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A mixed methods evaluation of the effectiveness of a nurse-led palliative care intervention for HIV positive patients on ART in Mombasa, Kenya

A thesis submitted to King's College London
for the Degree of Doctor of Philosophy

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Abstract

Background

People living with HIV (PLWH) accessing antiretroviral therapy (ART) report worse mental well-being than general populations and those with other chronic conditions.

Aim

To evaluate the effectiveness of a nurse-led palliative care intervention on the mental well-being of PLWH on ART in Kenya compared with standard care.

Methods

A randomised controlled trial (RCT) with longitudinal monthly follow-up over five time points and qualitative exit interviews was conducted. The primary outcome was psychological quality of life (Medical Outcome Study-HIV), with secondary outcomes being psychiatric morbidity, worry and ability to share feelings. Eligible participants were adults on ART reporting moderate to severe pain or other symptoms. Analyses included ordered logistic regression at monthly time points and multilevel modeling to identify intervention benefit. A purposive subsample of 30 participants across both study arms were selected for qualitative interviewing. Thematic analysis explored active ingredients of the intervention and experiences of study participation.

Results

16% of all patients screened were eligible; 56% refused to participate. 120 patients were recruited (mean age 39, SD 8.9, 81% female) and equally randomised to each study arm. Quantitative data analysis found significant benefit of the intervention in psychological quality of life (coefficient 0.59 (CI 0.12-1.07), $p=0.015$), psychiatric morbidity (coefficient -0.50 (CI -0.96 to -0.03), $p=0.035$) and ability to share feelings (coefficient 0.92 (CI 0.28-1.56), $p=0.005$). Qualitative analysis identified three active ingredients of the intervention: insight and understanding, medication and time. Unresolved physical, social and financial problems were identified as barriers to improvement. Aspects of study participation found to improve mental health and well-being were compassionate care, social support, communication, and material support.

Conclusion

The intervention was effective in improving mental well-being through health information, symptom relief and enabling participants to articulate problems. Aspects of study participation benefited participants in both study arms, highlighting unmet needs of PLWH.

Candidate's statement: The origins of this PhD thesis and my contribution

The data used in this thesis are from the Kenyan TOPCare trial, which was an RCT of a nurse-led palliative care intervention in Mombasa, Kenya in collaboration with the University of Nairobi, the Kenyan Hospice and Palliative Care Association (KEHPCA), Bomu Hospital and Coast hospice in Mombasa. An identical trial was also conducted in Cape Town, South Africa.

The trial design was confirmed, ethical approval gained and research nurses appointed and trained before I began in my role as a PhD student. I attended the study launch in Cape Town, South Africa, in March 2011, where I participated in the training of the researchers working in Kenya in collaboration with the Research Associate who had designed and managed the trial to that point with Dr Richard Harding (see Appendix 1 for study timeline).

I project managed the Kenyan study site during data collection; designing data monitoring tools to monitor progress and data quality and identifying and managing problems as they arose. I conducted a fact finding site visit in July 2011 in response to some concerning data through which I identified that there were initial issues at the study site regarding implementation of the recruitment protocol. This required the study to stop recruiting participants and restart again after I had addressed these concerns, to ensure a high standard of data quality, in collaboration with the clinic management and the study team in Mombasa. I maintained weekly contact via Skype with the study team in Mombasa throughout data collection: monitoring progress and supporting the study team (see Appendix 2 for Skype Checklist for site call). I also checked the data base weekly, performing coherency checks and referring back to the researcher for clarification of inaccuracies.

The concept of the PhD thesis arose from my interest as a nurse in the mental health and well-being of the patients, which was at that time the secondary outcome of the TOPCare trial. I developed the thesis aim, objectives and research questions, and conducted a systematic review of the psychological and social problems of people living with HIV (PLWH) on ART (Appendix 3). I wrote the analysis protocol, and carried out all the analysis. All interpretations and conclusions are my own.

My specific contribution to the TOPCare trial was to add a qualitative component, making it a mixed methods evaluation. I successfully applied for funding for the qualitative component of the trial, which included writing the qualitative data collection protocol and a projected budget, obtaining ethical approval from Kings College London Research Ethics Committee and the Kenyan Medical

Research Institute (KEMRI) (Appendix 4), and designing the qualitative data collection tools and a qualitative data collection training pack for the researcher. I subsequently managed the transcription and translation of the interviews, in preparation for analysis.

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Publications and presentations

Research publications

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Lowther K, Simms V, Selman L, Sherr L, Gwyther L, Kariuki H, et al. Treatment outcomes in palliative care: the TOPCare study. A mixed methods phase III randomised controlled trial to assess the effectiveness of a nurse-led palliative care intervention for HIV positive patients on antiretroviral therapy. *BMC Infectious Diseases*. 2012; 12:288.

Lowther, K., Higginson, I., Simms, V., Gikaara, N., Ahmed, A., Ali, Z., Afuande, G., Kariuki, H., Sherr, L., Jenkins, R., Selman, L., Harding, R: A randomised controlled trial to assess the effectiveness of a nurse-led palliative care intervention for HIV positive patients on antiretroviral therapy: recruitment, refusal, randomisation and missing data. *BMC Research Notes* 2014 7 (600)

Research presentations at scientific meetings

Lowther K., Harding R., Selman L., Higginson I.J., Simms V., Ahmed A., Gikaara N., Afuande, G., Zuhura F.J., Sherr L., Kariuki H., Ali, Z., Psychosocial outcomes of a Phase III randomised controlled trial (RCT) to assess the effectiveness of a nurse-led palliative care intervention for HIV positive patients on antiretroviral therapy (ART). *European Association of Palliative Care Conference* (poster presentation, abstract number P2-046) Prague 2013

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Acronyms and abbreviations

APCA	African Palliative Care Association
ART	Antiretroviral Therapy
APOS	APCA African POS
BDI	Beck Depression Index
CES-D	Centre for Epidemiological Studies depression tool
HADS	Hospital Anxiety and Depression Scale
HIC	High Income Countries
HIV	Human Immunodeficiency Virus
HIV/AIDS	Human Immunodeficiency Virus or Acquired Immunodeficiency Syndrome
KCL	Kings College London
KEHPCA	Kenyan Hospice and Palliative Care Association
KEMRI	Kenyan Medical Research Institute
LMIC	Low and Middle Income Countries
MINI	Mini International Neuropsychiatric Interview.
NHS	United Kingdom National Health Service
PEPFAR	(United States) President's Emergency Program For AIDS Relief
PLWH	People living with HIV/AIDS
POS	Palliative Outcomes Scale
PROM	Patient Reported Outcome Measure
SSA	sub-Saharan Africa
UNAIDS	United Nations Program for HIV/AIDS
UNICEF	United Nations Children's Fund

Introduction

Despite much medical and scientific progress, HIV infection remains a significant and persistent problem, with approximately 35 million people living with HIV (PLWH) worldwide in 2012 (1). Infection erodes immunity, increasing susceptibility to infection, and if left untreated leads to premature death from opportunistic infections or AIDS-associated cancers (2). Treatment consists of a combination of three medications that control virus replication, but are as yet unable to completely eradicate it (3). Infection is highly stigmatised, with socio-cultural associations of immorality, promiscuity and deviance (4, 5).

The experience of living with HIV has been revolutionised by recent medical advances in the field of HIV treatment and care, which have transformed the prognosis from a potentially imminent, physically painful and socially isolated death, to that of a chronic condition, manageable with a combination of medications and monitoring of immune functions (6, 7). These developments have also reduced the infectiousness of HIV, thus reducing HIV transmission and prompting further policy changes to widen eligibility criteria (8). This has led international stakeholders to declare the possibility of a future AIDS free generation (9, 10).

Clinical research conducted in the UK, USA and sub Saharan Africa (SSA) has highlighted the persistent symptom burden experienced by PLWH on ART. A cross sectional study conducted to assess the symptom burden of PLWH on ART in South Africa revealed continued high prevalence of psychological symptoms including sadness, irritability and worry, in addition to physical symptoms such as numbness and pain (11). These findings have been replicated in clinics in the UK (12) and the USA (13, 14), all describing a similar situation of unaddressed psychological and physical symptoms in PLWH on ART. Of prime concern is the prevalence of depression and anxiety in PLWH established on ART, which is greater than in the general population, and also greater than prevalence in patients with medically similar chronic conditions (15).

Arguably related to this, HIV-associated stigma remains a significant challenge to PLWH and its reduction is a key concern of the HIV clinical, academic and activist communities, as it reduces HIV testing, access to treatment and treatment compliance, in addition to being negatively associated with quality of life and mental health and well-being (15-18). It is important for enhanced quality of life for PLWH, and also clinically due to associations between poor mental health and non-adherence to treatment, which then leads to treatment failure (19). A solution to these problems in terms of healthcare provision is therefore urgently needed.

Kenya is targeted in a recent UNAIDS and WHO policy document, which identifies thirty countries where they state that ART scale up should reach 90% of the eligible population by 2015 (9). Concerns have been raised that this will place increased strain on fragile healthcare systems, particularly in low and middle income countries (LMIC); which is especially a concern in the context of higher survival rates of PLWH which indicate provision of high quality services for a longer time period (20, 21). Recent data reporting increased patient loss to follow up and pharmacies with inadequate supplies of medication for patient demand in the context of rapid programme scale up in Kenya have compounded these concerns (21).

Therefore despite a growing body of knowledge on the symptom burden of PLWH on ART, there is limited evidence for the effectiveness of models of care to address these symptoms. This is particularly troubling as the population of PLWH on ART is, firstly, continuing to grow with increased eligibility for ART will continue to require high quality, long term HIV treatment and care whilst stable on treatment (9), and secondly, is mostly being treated in the context of a rapid scale up of ART provision and in healthcare systems under strain in LMIC (21). As Kenya has been appointed a target country in the Treatment 2015 policy document, is apparent that Kenya is at the forefront of developments which will shape the future of the HIV epidemic, and therefore especially as a LMIC, is an ideal context in which to trial a model of care for PLWH.

Whilst a holistic approach such as palliative care has been suggested to improve the quality of life for PLWH (22), the effectiveness of such an approach has not yet been trialled experimentally, and thus there is no evidence base for programme development. In SSA, holistic care for patients and families is provided through informal networks, traditional healers, or in medical contexts for patients diagnosed with life limiting conditions through palliative care (23). Palliative care is a growing movement in SSA, with an increasingly skilled workforce and an increasing body of research evidence defining the need and justifying palliative care in SSA (23-26). As such, the model of palliative care as a holistic and culturally appropriate approach is a potential solution to the problem of a model of care for PLWH to help manage the multidimensional needs of this chronic condition in Kenya and SSA.

The aim of this thesis is to evaluate the effectiveness of a nurse-led palliative care intervention for PLWH on ART in Kenya, in terms of outcomes for mental health and well-being, and to identify the active ingredients and mechanisms of action associated with the intervention. Through this research, a locally sourced, holistic solution to this growing problem is evaluated using a mixed methodology (27), with public health, academic and clinical implications and findings of relevance for PLWH in Kenya, SSA and worldwide.

1. Background

This chapter will describe the external macro and micro structures which influence the mental health and well-being of PLWH and the delivery of their care. This will include a discussion of the international epidemiological and political context with a focus on Kenya and comparable LMIC in SSA.

The chapter also includes an overview of the concepts used in this thesis: HIV and its treatment, mental health and well-being, mental health and HIV, and current models of care for PLWH. It will conclude with a summary of the evidence which suggests a modified model of the palliative care approach may address the problems identified.

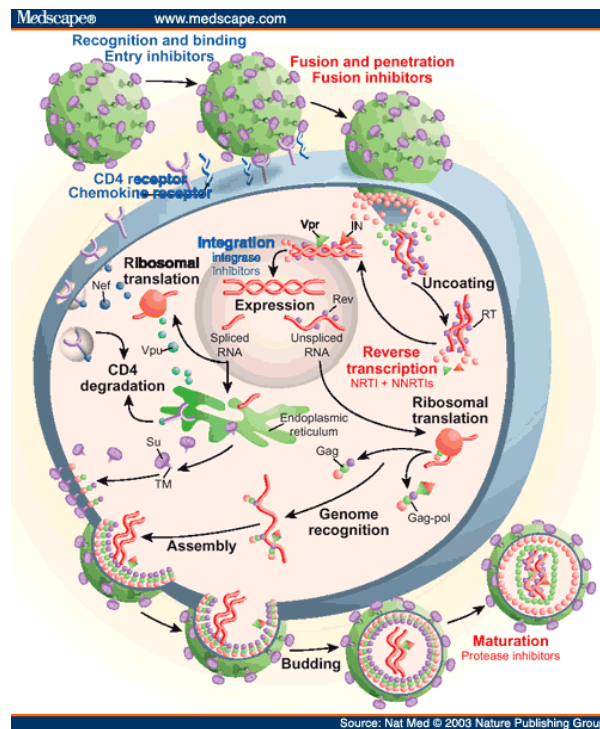
1.1. HIV

HIV belongs to a group of viruses called retroviruses and was first identified in the early 1980s. These first cases of HIV, before the virus was isolated, were detected when previously healthy individuals presented with immune deficiency and died of opportunistic infections (OI) (2). The virus is transmitted through sexual contact or from mother to child during pregnancy, childbirth or lactation, or through sharing contaminated injecting equipment. It replicates within the body in immune cells called CD4 cells, which become virus 'factories' before dying and releasing new copies of the HIV virus. This death of CD4 immune cells leads to immune suppression and death if not interrupted.

There are six classes of anti HIV drugs, called anti-retrovirals (ARV). They work at different stages of the cell cycle to interrupt viral replication, demonstrated in Figure 1 in red type. The first, most commonly used group are the nucleoside reverse transcriptase inhibitors (NRTIS: Zidovudine (AZT), Lamivudine (3TC)), the second, the non-nucleoside reverse transcriptase inhibitors (NNRTI: Nevirapine (NVP), Efavirenz (EFV)) and the third, the nucleotide reverse transcriptase inhibitors (Tenofovir) which all interrupt the reverse transcriptase enzyme, essential in viral DNA replication. Protease inhibitors (PI: Nelfinavir, Lopinavir), often boosted by a low dose of Ritonavir, block protease, an enzyme essential in the maturation of the new virus cell. Newer ARVs include Maraviroc, a CCR5 inhibitor which blocks the HIV virus from attaching to the CD4 cell thus preventing it from entering and replicating, and Raltegravir, an integrase inhibitor which blocks the action of the enzyme integrase in viral DNA reproduction (28). Fusion inhibitors are less commonly used as they are administered by injection sub-cutaneously, but their mechanism of action is to prevent the HIV cell fusing with the CD4 cell, preventing the cell cycle from beginning.

Background

Figure 1 HIV replication cycle, highlighting ART mechanisms of action (Source: Medscape.com)



Antiretroviral therapy (ART) is a combination of three medications from more than one of these different classes of drug. Working in combination, they suppress viral replication, addressing the many and various mutations which create viral resistance, and control the viral load.

Diagnosis with HIV indicates the presence of HIV virus in the body. High levels of HIV virus deplete the immune system as described, making the body more susceptible to certain cancers and OI, which when diagnosed in the presence of HIV are termed AIDS-defining diseases. Having an AIDS defining disease means that the patient can be described as having AIDS, although this term is less commonly used, now that the progression from HIV to AIDS is reversible and no longer as predictable.

1.1.1. Global HIV epidemiology

By the end of 2012, it was estimated that 35.3 million people (95% confidence interval 32.2-38.8 million) globally were living with HIV (29). Worldwide incidence of HIV infection has fallen by 33% in adults and 52% in children since 2001, and was reported as 2.3 million in adults (1.9-2.7 million) and 260 000 (230 000-320 000) in children in 2012 (29). Since its peak in 2005, global AIDS-related mortality has fallen by 30%, from 2.3 million deaths in 2005 (2.1 million–2.6 million), to 1.6 million in 2012 (1.4-1.9 million) (29). This pattern of peak and subsequent decline in AIDS-related mortality occurred in North America and Western and Central Europe in 1995, and much later in SSA, in 2005, corresponding with the widespread introduction of ART (30). The early benefits of ART in Europe on

new infections and mortality are clearly documented by the EuroSIDA cohort study, with the incidence of diagnosis with an AIDS defining illness falling by 8% per six month period from the introduction of effective ART in September 1998 to 2002 (31). ART reached 9.7 million people in LMIC in 2012, representing 61% of all eligible patients under the 2010 WHO guidelines, and 34% of all eligible under the 2013 guidelines (29).

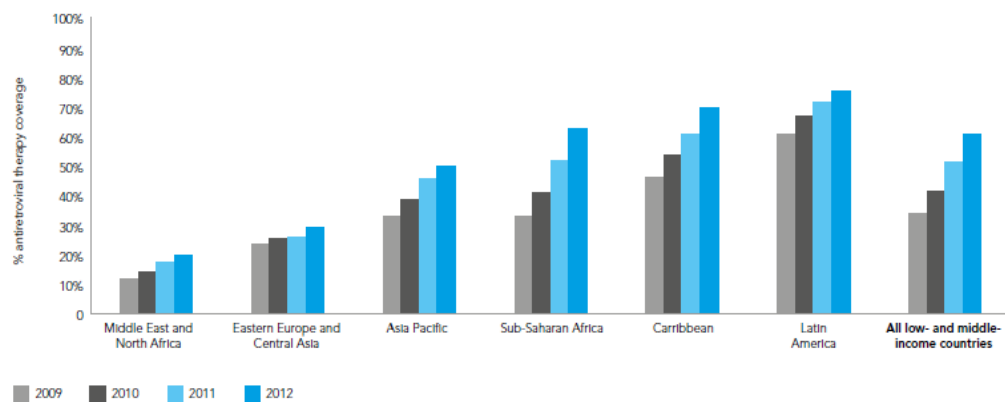
This peak and subsequent decline in mortality globally has led to slight increases in prevalence in some areas and stable prevalence elsewhere, as people survive for longer due to the introduction of effective treatment (30). The prevalence in SSA has declined, due to persistent high mortality and a 25% reduction in incidence (30) which itself resulted from public health campaigns for behaviour change (19, 20).

1.1.2. Antiretroviral therapy

1.1.2.1. Eligibility and access to ART

Since the introduction of highly active ART in 1996, made accessible in LMIC by 2004, progress has been made in increasing the proportion of eligible patients receiving ART (Figure 2).

Figure 2 Percentage of eligible people receiving ART in LMIC, (according to 2010 WHO guidelines). Taken from UNAIDS 2013 (29)



In the past ten years international policy has increased the CD4 threshold for initiation of ART four times (2004, 2006, 2010 and 2013), due to research evidence indicating that initiation at earlier stages of HIV, before the immune system has been severely damaged, can lead to increased likelihood of survival and a decrease in complications (32-35). In addition, new evidence indicates that when given as pre-exposure prophylaxis, or to HIV sero-negative sexual partners of HIV sero-positive patients (known as treatment as prevention or TAsP), ARVs reduce the risk of transmission of HIV to almost zero (36, 37). This has public health and epidemiological implications for the

reduction in incidence of HIV, and has led to the most recent guidelines recommending that treatment should be initiated for those with a CD4 count of less than 500 cells/cm³, those co-infected with TB, or hepatitis B and those in sero-discordant relationships (33). These changes have contributed greatly to increases in numbers of patients eligible for ART, placing pressure on healthcare systems to provide adequate care(21) (20).

1.1.2.2. **Medical outcomes of ART**

The introduction of ART prolongs life, leading to an increasing population of PLWH. People on ART are expected, once on effective treatment, to live socially and economically productive lives, managing HIV as a chronic disease.

Analysis of mortality data in nine industrialised countries found that mortality rates of HIV positive patients, who have commenced ART and survived for the initial 6 months (when risk of death is higher), are comparable to that in patients with other chronic conditions (38). In addition, causes of mortality in PLWH are no longer mostly due to HIV related infections or cancers (only 16.1% of mortality due to AIDS related illnesses in HIV positive cohort from Switzerland (39)). Excess mortality might therefore be further prevented by earlier detection of HIV and timely initiation of ART.

More recent data from the US and Canada describe how, while differences across baseline CD4 count, race, gender and transmission risk group still occur, a person infected with HIV at age 20 on ART and living in the US or Canada can expect to live to the age of 70 (6). Increases in life expectancy are not limited to the global north. In 2011, a study from Uganda identified an almost normal Ugandan life expectancy (55 years), with variation due to immunity at diagnosis and ART initiation (7). Data from South Africa has shown that provided patients initiate ART before their CD4 count drops below 200cells/cm³, they can expect to live for 80% of the normal life expectancy in South Africa (40).

These data suggest that, in the context of early initiation and easy access to ART, in the near future, AIDS will rarely be seen in the context of controlled HIV virus, and the pandemic will be no longer seen as a catastrophe (41). However, whilst this era of HIV management is termed the era of treatment availability, with only 34% of the 28.6 million people currently accessing ART, according to the 2013 WHO guidelines (8, 29), some authors suggest it might better be termed the era of treatment possibility (41).

Improvements in life expectancy, whilst extremely positive, create new medical challenges for the HIV community. The model of care for PLWH must now manage the co-morbidities, or complications as a result of ageing, opportunistic infections, and symptoms from previous more toxic ART regimens in addition to the psychological and social problems associated with HIV infection. In addition, this must be provided successfully within the structural and social challenges of often fragile healthcare systems, to provide life-long treatment for millions of people (42).

1.1.2.3. Implications of the recent changes to ART access guidelines

In July 2013, UNAIDS, WHO, PEPFAR and the Global Fund launched a programme called Treatment 2015. The stated aim of this programme is to increase coverage of ART to reach a target of 15 million eligible PLWH by 2015, as part of a global public health strategy to control the HIV pandemic (9). This framework has identified 30 countries where there is unmet need for ART provision. If 80% of people eligible for treatment within these countries are provided with ART, this will account for 90% of the 15 million target (9). With the introduction of treatment for prevention within the 2013 initiation guidelines, and anticipated reduction in new infections (37), this programme aims to lay the foundation for the end of the AIDS epidemic (9). Its authors describe benefits in terms of public health, economics, and social justice, and anticipate the prevention of an additional 3 million AIDS deaths and 3.5 million new infections by 2025, compared with the previous 2010 guidelines (9).

The Treatment 2015 document states that the focus on provision of ART should not be at the expense of quality care, which should continue to be provided by efficiently streamlining HIV services with other services for chronic conditions and by increasing partnerships between institution and community care, rather than the provision of extra resources (9). It advocates that funding should increasingly be provided by national governments and not international donors, which has raised concerns in the current economic climate that this may restrict the ability of certain countries to provide high quality holistic care (9). The implications of this for theoretical models of HIV healthcare provision are addressed below.

1.1.3. Current models of HIV healthcare provision for mental health and well-being

Current HIV healthcare provision is described in international policy literature as consisting of three components: treatment, care and support. Treatment refers to the provision of ART by institutional providers, with care and support typically referring to psychological and social aspects of care: “a comprehensive set of services, including psychosocial, physical, socio-economic, nutritional and legal

care and support” (UNAIDS) (43). The 2010 UNAIDS strategy goes on to say that care and support is essential for well-being and should be offered from diagnosis and throughout the disease trajectory.

In high income countries (HIC), HIV treatment guidelines emphasise the importance of psychological and social support of people with HIV, as part of the HIV care package, particularly with reference to ensuring good adherence to ART (44, 45). These guidelines model good mental health and psychological well-being for all people with HIV, access to psychological support, involvement of PLWH/AIDS, support at diagnosis, assessment to identify needs, access to competent practitioners, co-ordination of support and evidence-based practice (45).

Guidelines for HIV care and support (beyond provision of ART) in SSA are less consistent. The Kenyan National Guidelines for ART include psychosocial care as an essential intervention for people with HIV, recognising the psychological and social impact of a HIV positive diagnosis (46). In South Africa, the guidelines suggest annual health education updates, but only on nutrition and contraception, with a more comprehensive psychological assessment in the event of treatment failure and virological rebound (47). The ability of the healthcare system in any country to provide holistic healthcare is dependent on political and economic support and the extent to which the resources available can address the burden of disease. Psychological and social support of PLWH is often the more neglected aspect of care, as policy makers often assume that this will be provided by family members, more specifically women, particularly within LMIC (43, 48). This valuable resource of care has become more precarious and strained, as the effects of HIV break down community and family units, increasing pressure on the remaining family members (49).

Globally, the epidemiology of the HIV pandemic appears to be shifting from acute crisis to chronic management of disease (50). This shift will require changes in healthcare provision in terms of care and support, in response to the changing needs of PLWH. Currently, due to persistent financial and logistical constraints, health systems often only provide the minimum of physical care and provision of ART in low resource settings (51, 52). From a patient’s perspective, moving from crisis to chronicity requires economic and social support to return to previous standards of productivity, economic contribution and positive mental health and well-being, after a prolonged period of ill health (50). This is particularly relevant in light of international pressure on national governments to increase access to ART and a simultaneous decrease in resources provided to meet these needs.

1.2. Mental health and well-being

1.2.1. Terms and definitions

The concept of health was defined by the WHO in 1948 as “the state of complete physical, mental and social well-being and not merely the absence of disease or infirmity” (53). In the context of this study three aspects of this definition are important in understanding mental health: positive mental health is integral to health, mental health is more than the absence of mental illness, and mental health is closely associated with physical health and well-being (54).

The WHO elaborated on their definition of health in 2001 to further define mental health as “a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community” (55). This indicates that mental health and well-being contribute not only to the functioning of the individual but also to the community, and are more than the absence of psychopathology. Mental illnesses such as major depression and anxiety are recognised consequences of unmet mental health needs. In this thesis the framework for understanding these processes will be that developed by the WHO in collaboration with the Victorian Health Promotion Foundation and the University of Melbourne (56). It describes the key determinants of mental health as: social inclusion, freedom from discrimination and violence and economic participation (56).

1.2.2. Determinants of mental health

It is argued that mental health is at a conceptual crossroads, where previously mental health was situated within the medical model, mental health promotion is now moving into a more multidimensional approach, embracing the social determinants of mental health (56). In a similar way, 30 years ago cardiac health promotion care was firmly situated in the medical model, and now invokes advocacy of physical exercise, tobacco use cessation, nutrition and anxiety management (56). Increasingly, academics and professionals within the field of mental health cite evidence that mental health and well-being are determined and should be addressed by tackling social, environmental and economic factors (56-58). These factors are listed as: social inclusion and access to socially supportive networks; stable and supportive family, social and community environments; access to a variety of activities; having a valued social position; physical and psychological security; opportunity for self-determination and control of one's life; and access to meaningful employment, education, income and housing (56).

These factors have been incorporated into an evidence based framework for the promotion of mental health and well-being as discussed by VicHealth (an Australian foundation for promoting good health and preventing chronic disease) in collaboration with WHO and the University of Melbourne (Figure 3) (56).

Figure 3 VicHealth's framework for the promotion of mental health and well-being

Key determinants of mental health and themes for action		
Social inclusion	Freedom from discrimination and violence	Economic participation
Supportive relationships Involvement in group activities Civic engagement	Valuing of diversity Physical security Self determination and control over one's life	Work Education Housing Money
Intermediate outcomes		
Individual	Organisational and community	Societal
Increased sense of : Belonging Self esteem Self determination and control	Accessible and responsible organisations Safe supportive and inclusive environments	Integrated and supportive public policy and programmes Strong legislative platform Resource allocation
Long term benefits		
Less anxiety and depression Less substance abuse Improved physical health	Improved productivity at home, work and school Less violence and crime	Reduced health inequalities Improved quality of life and life expectancy

This framework can be described as an intersectional approach, acknowledging the overlap and interdependency of social, psychological and economic determinants on positive mental health and well-being, developed on the basis of international research evidence of the effect of addressing these determinants (56). This interdependence between the domains of well-being highlights why the framework is particularly appropriate for conceptualising positive mental health and well-being in this thesis, as it has resonance with the Biopsychosocial and holistic understanding of health and well-being, central to the palliative care approach on which the nurse-led intervention to be evaluated is based (59).

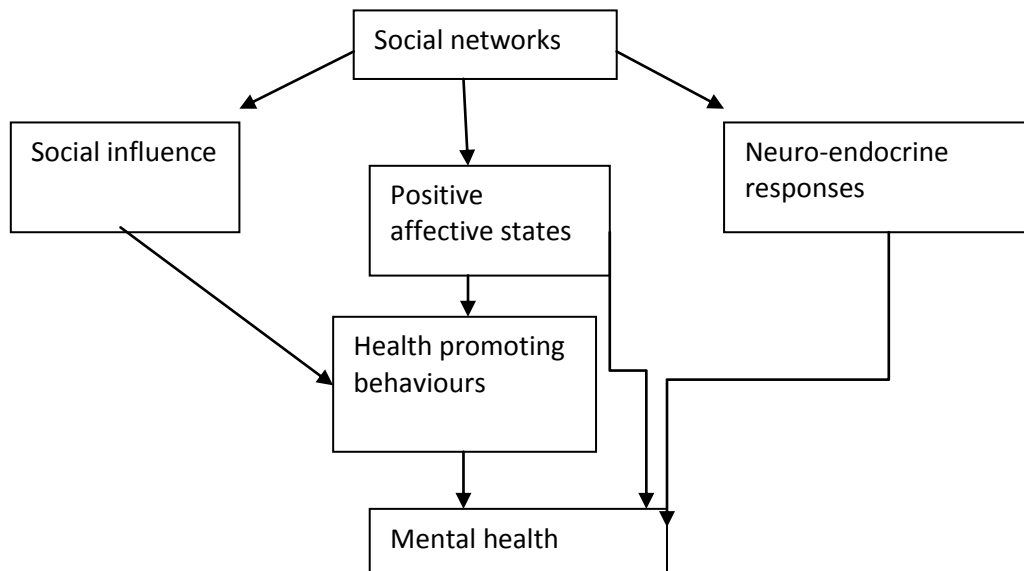
The following sub-sections expand on each of the key determinants of health in the model adopted for this thesis.

1.2.2.1. Social inclusion

A review conducted for the National Institute for Health and Clinical Excellence (NICE) in the UK identified a range of factors which were protective of mental health (57). These included social capital and strong social networks, social inclusion, trust among community members and educational achievement (57). Decreased social connectedness is negatively associated with quality of life, mediated by negative perceptions of stress and stressful experiences.

To describe the effect of mental health and social networks, the model developed by Kawachi and Berkman is useful, and describes the direct mechanism of influence of social networks or ties on mental health (Figure 4)(60).

Figure 4 Main effects model of social networks and mental health. From Kawachi and Berkman (60)



Kawachi and Berkman describe how social networks can improve mental health through educating and informing an individual of health promoting behaviours, such as the effect of exercise in groups, or why it is important to stop smoking. Social networks also increase positive affective states in the individual, by inducing feelings of belonging and security, in addition to increased self worth. They suggest that these positive states positively affect mental health through motivation for health promoting behaviours and self care, such as eating and drinking in moderation, or taking regular exercise, in addition to modulating neuro-endocrine responses to stress. Being located within a social structure increases an individuals' access to social support, such as informal psychological first aid, which protects against more serious distress (60).

Separate studies show that the presence of protective social factors such as belonging to social networks etc, is associated with individual factors identified as protective to positive mental health: feeling respected, valued and supported, and having a sense of hopefulness (57). Individual level risk factors included lack of emotional resilience, genetic predisposition, family history of psychiatric disorder, childhood neglect or abuse, bereavement and being a long term carer (57).

1.2.2.2. **Freedom from discrimination**

The evidence suggests that a society which encourages freedom from discrimination, diversity, freedom from violence and self determination and control over one's life, is a society which is promoting positive mental well-being (56).

Discrimination affects mental well-being in several ways. Often it originates in stigma, which is defined as an attribute, behaviour or reputation which is socially discrediting (61). Stigma is a complex and multifaceted concept, expressed and experienced differently in different cultural contexts. It can be conceptualised as 'enacted' in the form of discrimination, 'normative' (a set of accepted values embedded in cultural norms), or 'internalised', meaning that the stigmatising messages are accepted (62). There are three functions of stigma in society: to exploit and dominate those in a less powerful position, to enforce social norms promote social stability; and to distance perceived threat of contamination, for example from infection or immorality (63). Stigma highlights the perceived threat of diversity to physical security.

When individuals are discriminated against, and their physical security or freedom from violence cannot be guaranteed, increased psychological and behavioural problems such as anxiety, depression, alcohol abuse and suicidal behaviour are reported (64).

A recent systematic review and meta analysis of the literature found that experience of stigma and discrimination is associated with heightened stress response is related to non-participation in healthy behaviours and participation in unhealthy behaviours, and is strongly and consistently associated with psychological distress (65). This effect has been documented in immigrant populations who experience discrimination on a racial basis (66-68), and in PLWH, (69-71).

Discrimination can also reduce access to healthcare services and reduce compliance with treatment, as potential patients fearing the stigmatising label of a diagnosis, distance themselves from potential sources of help (72). This exacerbates pre-existing problems and is a barrier to recovery.

1.2.2.3. Economic participation

The effects of economic participation extend to the effects of work, education, housing and money on mental health and well-being (56).

Unemployment was associated with psychological distress, in a cohort study from Canada (73), and in a meta-analysis of international literature on the effects of unemployment and lack of economic participation (74). A separate review found that there is also evidence that those who are employed but who experience job insecurity also have increased psychological distress, psychosomatic complaints and physical strain (75).

Findings from a study from the US identified that in areas of low unemployment, respondents with a college education who had previously been employed, reported the highest levels of depression and subjective physical health status, with two main causes: distress due to financial strain, or due to damage inflicted by unemployment status on participants' sense of self (76). Self-image and self-efficacy were also apparent in evidence from New Zealand, where students with financial debt reported decrease psychological well-being when they perceived that they would be unable to manage the debt, associated with sense of control and self-esteem (77). This association between psychological distress and perceived socioeconomic status and deprivation was also reported in two separate studies from the US (78) (79).

Respondents from both urban and rural areas in South Africa described the practical side of life such as the importance of housing, money and a job, when asked to evaluate the concept of human well-being (80), highlighting their understanding of the importance of economic and material participation to human well-being.

1.2.3. Mental health and well-being in HIV

Internationally, the experience of living with HIV is associated with a burden of unmet psychological and social needs. A systematic review of mental health problems in HIV patients in India identified high prevalence of clinician-rated depression, post-traumatic stress disorder, general distress and anxiety, substance abuse and general psychiatric morbidity above population norms (81). In Africa, a recent systematic review found 44% to 58% of all patients with HIV have psychological problems, most commonly depression (82). Furthermore, mental health problems in PLWH were associated with poverty, unemployment and poor educational attainment (82). A recent comparison of health related quality of life for adults living with and without HIV in the UK found that, despite being on ART and having an undetectable viral load those with HIV reported significantly worse health related

quality of life, more specifically in terms of anxiety and depression, mobility, self-care, usual function and pain (83).

In addition to impaired quality of life, unaddressed psychological and social problems have potentially severe clinical implications. A recent meta-analysis of international data identified a strong and consistent negative association ($n=95$ studies, $p < 0.0001$) between depression and adherence (19). Because patients must achieve optimal adherence ($>95\%$) to control the virus and avoid viral resistance and associated outcomes (treatment failure, increased infectiousness, morbidity and mortality), this association presents a very real threat to the success of international progress in controlling the epidemic (3, 84, 85).

Whilst regional and whole patient population reviews exist for depression, anxiety and experience of stigma in HIV patients, the international literature has not yet been systematically reviewed to examine the problems experienced by HIV positive patients, specifically established on ART. Understanding the extent of these problems in this growing cohort of PLWH on ART is extremely important both in terms of patient quality of life and the future implications for control of the pandemic.

To review the data in the literature of the prevalence of psychological and social needs experienced by PLWH on ART, I conducted a systematic review of the peer reviewed literature, in line with the PRISMA statement (86) and guidelines from the NHS Centre for Reviews and Dissemination (87). This review was published in the International Journal of Nursing Studies and can be found in full in Appendix 3, where the full method including search strategy, search terms, inclusion and exclusion criteria, data management and analysis are reported (15). The results summarise the prevalence of anxiety, depression and experience of stigma in HIV positive people on ART. The presence or absence of the experience of stigma was included as an indication of the social problems associated with a diagnosis of HIV.

The data is reported using weighted mean prevalence calculated using a data quality score following Loney *et al* (88), attributing more weight to prevalence reported from studies of higher quality.

1.2.3.1. Depression

A total of 62 retained citations reported mean sample prevalence for depression (summarised in Table 1-1). The range of reported depression prevalence is illustrated in Figure 5 for all retained citations and by country income status.

Table 1-1 Summary of depression prevalence for all citations and by country income status

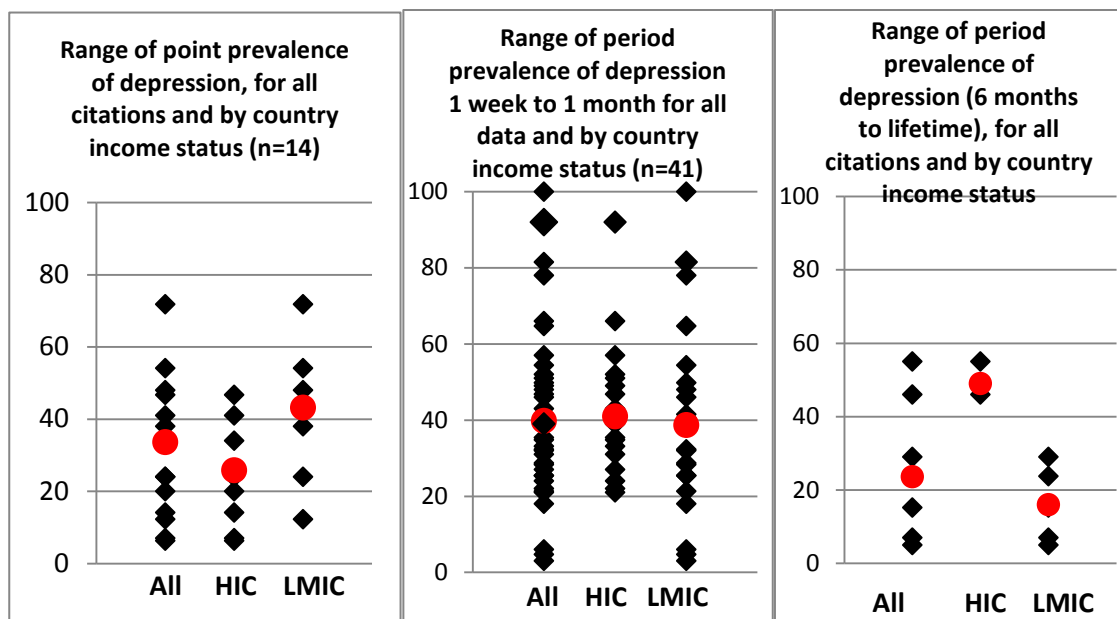
Depression (all means weighted by data quality score following Loney (88))			
	Mean (sd)	HIC (sd)	LMIC (sd)
Point prevalence (n=14)	33.60 (19.47)	25.81 (15.21)	41.36 (21.42)
Included studies	(89-102)	(89-96)	(97-102)
Period prevalence of 1 week- 1month (n=41)	39.79 (21.52)	40.96 (17.08)	38.69 (25.07)
Included studies	(11, 103-141)	(104, 106, 107, 110, 116, 118-124, 128, 133, 136-138, 140)	(11, 103, 105, 108, 109, 111-115, 117, 125-127, 129-132, 134, 135, 139, 141)
Period prevalence of 6 weeks to lifetime (n=7)	23.61 (19.03)	49.0 (6.36)	15.99 (10.39)
Included studies*	(89, 99, 100, 117, 122)	(89, 122)	(99, 100, 117)

*Several studies contributed more than one prevalence period, e.g. lifetime, one year and 6 months, so numbers may not add up to total number of citations

This review identified a weighted mean of point prevalence of depression in people with HIV on ART across the citations of 33.6%, with a higher point prevalence of depression reported in LMIC (41.36%) compared with HIC (25.81%). Period prevalence, combining data over the past week to month was as expected, higher. The period prevalence weighted mean was 39.8% in all retained citations, 41.0% in HIC, and 38.7% in LMIC. Fewer studies reported rates for depression over the lifetime, or in the past 6 months, and so the data were merged to reports of depression in the longer term (6 months to lifetime). The difference in reported 6 months to lifetime depression comparing HIC and LMIC is noteworthy, although there was strong potential for bias due to the small numbers of papers reporting this data.

From the scatter plots several outliers are evident (Figure 5). These outliers appear to originate in more homogenous and possibly more unusual samples than the general HIV population. The data reporting 100% one-week period prevalence of depression was among mothers who were attending an outpatient clinic with their HIV positive children (113). The sample reporting 92% one-week period prevalence of depression was composed of people who used to inject drugs (119). The sample which reported 81.5% one-week prevalence of depression was composed of Rwandan women experiencing post-genocidal trauma (112). All of these samples might be expected to experience more psychological distress. Most other samples were more heterogeneous containing a mix of people who inject drugs, men who have sex with men, and other people from risk groups.

Figure 5 Scatter plots to illustrate the range and distribution of reported prevalence of depression

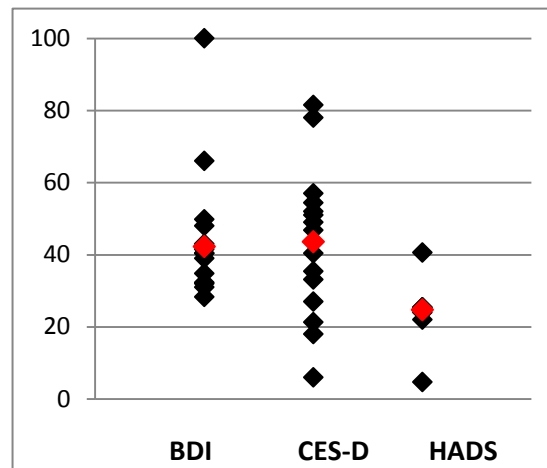


*All means weighted by data quality score ●=weighted mean

Prevalence for each risk behaviour group (people who inject drugs, heterosexual women, men who have sex with men, former plasma or blood donors) was not disaggregated in the studies identified; therefore a comparison of these sub-groups was not possible.

Analysis by measurement tool was possible only for point prevalence as period prevalence was not measured using standardised tools. The most commonly used measures were the Beck Depression Inventory (BDI), the Centre for Epidemiological Studies Depression tool (CES-D) and the Hospital Anxiety and Depression Scale (HADS). The range of prevalence and mean (again, weighted by data quality score) from the BDI, CES-D and the HADS data are presented in Figure 6. Data from the HADS appears to report lower prevalence of depression.

Figure 6 Range of 1-4 week period prevalence of depression by outcome measure



*All means weighted by data quality score ●=weighted mean

In this review, mean point prevalence of depression was 33.60% (sd 19.47) and 1-4 weeks period prevalence 39.79% (sd 21.52). The data for longer period prevalence was sparse and therefore the mean is less likely to be representative of the population.

The UK general adult population data for prevalence of depression ranges from 2.3% (142) to 8.1% (143). General population data from Nigeria reports a 5.2% point prevalence (144), the USA 9.5% 12-month prevalence (145), South Africa a 9.7% period prevalence for lifetime depression and 4.9% for the past 12 months (146), and in the Asia Pacific region figures stand at 1.3% to 5.5% current to 1 month prevalence of depression (147). The conclusion of this analysis is that prevalence of depression may be elevated in HIV positive people in comparison with international general population data.

Whilst this review identifies prevalence of depression in PLWH as 33.6%-39.8%, depression in other chronic conditions, which are incurable, and have physical symptoms requiring long-term management are comparatively lower. Patients with epilepsy for example, report a current or past year prevalence of 23.1% (148), multiple sclerosis patients (1 year period) 25.7% (149) and patients with diabetes a point prevalence of 28% in women and 18% in men (150).

This review further found decreased point prevalence in HIC 25.81% (sd 15.21) compared with LMIC 41.36% (sd 21.42)). Our data suggest that depression is higher in HIV positive people than in the general population, and that depression is more burdensome in LMIC than in HIC. This is compatible with recent international comparisons of the impact of depression on disability adjusted life years and years lived with disability, which indicate that the global burden of depression is higher in LMIC compared with HIC (151)

1.2.3.2. Anxiety

In total 14 papers reported the prevalence of anxiety in a study sample. Data are summarised in Table 1-2 and the range of reported prevalence illustrated in Figure 7.

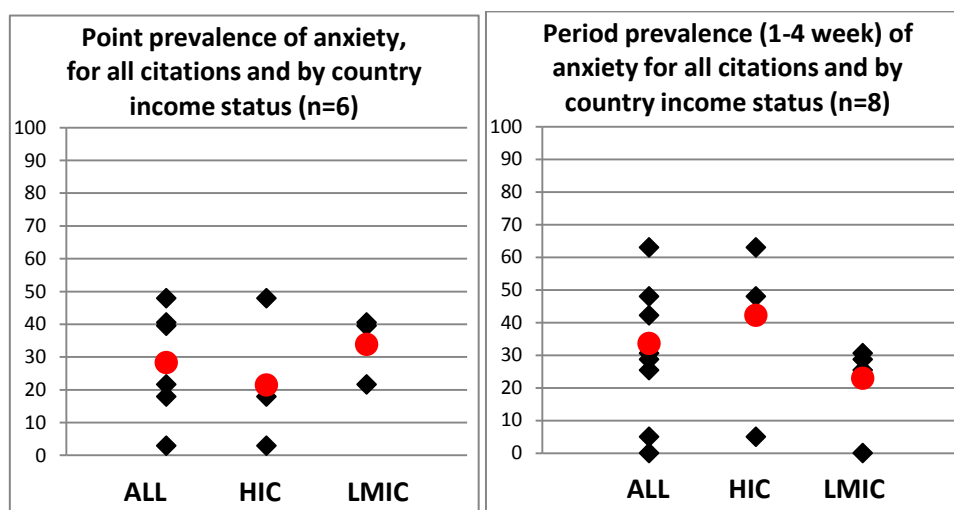
Table 1-2 Summary of prevalence of anxiety for all retained citations and by country income status

Anxiety (all means weighted by data quality score)			
	Mean (sd)	HIC mean (sd)	LMIC mean (sd)
Point prevalence (n=6)	28.38 (17.07)	21.53 (22.91)	33.92 (10.64)
Included studies	(94, 95, 102, 109, 152, 153)	(94, 95, 152)	(102, 109, 153)
1-4 weeks period prevalence (n=8)	33.59 (21.07)	39.55 (24.64)	21.18 (14.28)
Included studies	(14, 120, 125, 129, 132, 133, 139)	(14, 120, 133)	(125, 129, 132, 139)

The mean point prevalence of anxiety was 28.38%; this was lower in HIC (21.53%) compared with LMIC (33.92%). One to four weeks period prevalence was higher at 33.59%; this was higher in HIC (39.55%) compared with LMIC (21.18%).

The highest prevalence of anxiety was found in a study of women in a French cross-sectional study (63%) (133). Men in the same study reported a prevalence of 48% anxiety (133). The lowest prevalence of anxiety (0%) was in a Thai sample (132). The authors suggest that the low rate of anxiety could have been the result of strong social support among people with HIV/AIDS attending the clinic where recruitment occurred.

Figure 7 Scatter plots to illustrate the range and distribution of reported prevalence of anxiety



*All means weighted by data quality score ●=weighted mean

A recent systematic review identified a global prevalence of 7.3% anxiety in the general population, with a lower prevalence in African countries (5.3%) compared to Euro/Anglo cultures (10.4%) (154). The prevalence of anxiety disorders in the general population is 4.4% in the UK (142) and 18.1% in the US (145). Whilst there is variation in these figures, they are all lower than the prevalence identified in this review amongst people with HIV on ART: 28.38% (sd 17.07) mean point prevalence and 33.59% (sd 21.07) 1-4 week period prevalence.

The prevalence of anxiety among patients with HIV receiving ART identified in this review is also high in comparison with rates of anxiety among patients with other chronic conditions (diabetes 14%, cancer 15-23%, heart disease 10-50% (155)), suggesting that people with HIV/AIDS are at a higher risk of developing anxiety than other patients with chronic conditions, and the general population.

1.2.3.3. Freedom from discrimination - Stigma

Prevalence of stigma was reported in ten papers. Of these, seven reported an overall prevalence figure for the presence or absence of the experience of stigma in the study sample (see Table 1-3).

Table 1-3 Prevalence of experience of stigma across all citations and by country income status

	All data	HIC	LMIC
Point prevalence	41.92%, 46%, 82%	41.92%, 46%	82%
Included studies	(128, 156, 157)	(128, 156)	(157)
In the last 2 weeks	61.6%	-	61.6%
Included studies	(158)		(158)
From 'during the past year' to 'ever'	38%, 25.3%, 83%	83%, 38%	25.3%
Included studies	(159-161)	(159, 161)	(160)

The remaining three studies all used locally designed questionnaires, measuring different aspects of the experience of stigma. A study in Zambia focused on the experience of stigma specifically related to ART, reporting a prevalence of 16% (162). A national cross-sectional survey including HIV positive patients in France reported the percentage experiencing discrimination: 12.9% from relatives, 12.2% from friends and 16.3% from sexual partners (163). A study conducted in Botswana in 2006, before widespread access to ART, found that 12% of HIV patients had not disclosed their infection status to anyone. In the same study 27% of patients feared they would lose their job due to HIV, and 47% reported work-related difficulties due to HIV, mostly concerned with taking sick leave (164).

However, it cannot be assumed that the same cultural understanding or social construct of stigma is being reported across studies. In addition, differences between enacted, normative and internalised stigma are not differentiated in the retained citations (62). Although elements of these constructs are described by the stigma scales used in the identified studies, the assumed interactions between stigma and the experience of discrimination are not made explicit. For example, evidence suggests that the experience of stigma is often worse when patients have disclosed their serostatus, but levels of culturally acknowledged stigma in the society, which may dissuade people from disclosing and thus protect them from enacted stigma, have not been explored (156).

To add to the complexity, PLWH in HIC may experience 'compound' or 'layered' stigma, which exists along pre-existing social fault lines, relating to sexual orientation, intravenous drug use, or commercial sex work (165, 166). This creates difficulty when comparing experiences of stigma

between HIC and LMIC, where stigma is mostly associated with women and sexual morality, and raises the question of whether this kind of comparison is justified (167).

1.2.3.4. **Economic participation**

Prevalence data for economic participation for PLWH was not included in the systematic review, as the focus was on the psychological problems resulting from unmet mental health needs. However, the literature suggests that living with HIV is associated with decreased economic participation and economic hardship. For example, a study from Kenya found in the 18 months preceding their death, a cohort of HIV positive tea pickers were less productive than their HIV negative counterparts, took more sick or annual leave and were allocated less strenuous tasks which were less remunerative (168). This resulted in 16-17% decreased earnings. A cohort study from South Africa identified that households affected with HIV reported poorer health and were less affluent than those who were not, with rapid decreases in income and expenditure over a period of 6 months in households with HIV positive members (169). A epidemiological study in South Africa found that a HIV positive diagnosis increases the probability of being unemployed by 6-7%, with a greater effect seen in women, those in urban areas and those with less education, compounding pre-existing inequality (170).

Whilst the majority of data describe the situation in SSA before the widespread availability of ART, there is some data describing the effect of ART on economic participation. The effect of ART on the ability of PLWH to work and contribute economically was measured in a cohort of miners in South Africa in 2010 (171). They report a “Y shaped” response in absenteeism in HIV positive workers. This means that they returned to work with absenteeism rates comparable with their HIV negative counterparts once established on ART (171). Similar increases in economic productivity were reported in India in terms of economic participation, number of hours worked and individual income (172). Economic analysis of the impact of ART programmes suggests a range of return on investment in terms of economic activity from 81% -287% of the programme costs (173).

The literature describes the change from severe impact on employment and potential earnings before access to ART, to minimal impact if established on ART and in otherwise good health, without co-morbidities. This suggests a mitigating or buffering effect of ART on the effect of economic participation on mental health and well-being.

1.2.4. Summary of literature and evidence regarding HIV and mental health

The mental health and well-being of PLWH is impaired by their HIV positive diagnosis, with depression and anxiety higher in HIV positive people compared with the general population, particularly when they are physically unwell. This is concerning, not only as this represents a serious impairment in quality of life, but also as there is an identified strong and persistent association between depression and non-adherence to ART (19). Increased resistance to the available drug combinations due to non-adherence threatens the success of ART in terms of care for the resistant individual and of future options in primary and public health.

In addition, the review found that over half of patients on ART report experiencing stigma and/or discrimination, which has repercussions for health-seeking behaviour, retention in healthcare services and quality of healthcare received, in addition to the impact on mental health status (17, 174-176).

Prevalence of HIV will increase in SSA as mortality decreases with increased access to ART, which will result in increasing numbers of patients accessing already stretched healthcare systems. These patients will have medical needs for access to effective tolerable treatment to control their HIV virus and manage toxicities and opportunistic infections, in addition to increased risk of depression and anxiety and the difficulties of living with the virus in the context of continuing HIV related stigma.

International experts have called for the integration of mental health-promoting interventions into routine HIV care to benefit both mental and physical well-being of patients (177). Whilst these data highlight that this call is timely, pertinent and necessary, it is important to recognise that within a climate of increased pressure on governments to deliver on externally set targets for ART access, improving access to mental healthcare may be challenging. Potential solutions must therefore be feasible in terms of the human and financial resources available and have proven relevant evidence of effectiveness within this context.

There is therefore an urgent need to explore possible approaches to care in the context of increasing numbers of PLWH as a chronic condition, and therefore requiring long term management for complex psychological, social, and medical problems.

1.3. Kenya

This study is situated in Kenya, a country which borders Uganda, Somalia and Tanzania, and has a population of 44 037 656 (July 2013 estimate) and a median age of 18.9 years (178). Selected

demographic and health statistics for Kenya are presented in Table 1-4, with South Africa and the UK data presented to enable comparison.

Table 1-4 Comparison of demographic and health variables for Kenya, South Africa and UK

Country	Kenya	South Africa	UK
Life expectancy at birth (2012) ◇	69.4	53.4	80.1
Maternal mortality 2010 (/100 000 live births)	360	300	12
Adult HIV prevalence (15-49) (UNAIDS)	6.1% (5.9-6.3)	17.9% (17.3-18.4)	0.2-0.3%
Under 5 mortality rate (/1000 live births)†2010	85	57	5
GDP per capita 2011 (current US\$)	819	8090	38 918
% GDP spent on healthcare in 2010 *	2.1	3.9	8.1

◇Number of years a newborn infant could expect to live if prevailing patterns of age-specific mortality rates at the time of birth stay the same throughout the infant's life

†Probability of dying between birth and exactly age 5, expressed per 1,000 live births

* Current and capital spending from government (central and local) budgets, external borrowings and grants (including donations from international agencies and non-governmental organizations), and social (or compulsory) health insurance funds, expressed as a percentage of GDP.

Source: UNDP (179) and World Bank (180)

The UNDP states that Kenya has a gender inequality rating equivalent with low human development, indicating that economic development and gender equality are significant challenges, a finding restated by a recent US report on human rights in Kenya (180, 181).

1.3.1. HIV in Kenya

HIV is the lead cause of mortality in Kenya, accounting for 29.3% of all causes of mortality (followed by perinatal causes 9%, pneumonia 8.1% and tuberculosis 6.3%) (182). The Kenyan Government estimates HIV prevalence at 6.1% (1.6 million people) of the adult population, with 73% of all eligible PLWH on ART (2012) (183). The 2012 Government report describes the HIV care policy as a comprehensive approach, with food by prescription for malnourished patients and access to pain relief for all (although it is conceded that morphine is rarely available) (183, 184). The problematic shortage of health workers is also identified, in particular physicians (0.1 per 1000 people compared with 7.9 in the Euro zone), which may hamper the future success of any reforms (183).

The epidemic in Kenya is described as generalised, and transmission predominately occurs within stable partnerships (38%), men who have sex with men (20%), sex workers, their clients and their

partners (18%) and casual sex (15%)(183, 185). Point prevalence of HIV differs according to wealth, with increases from 4.6% in the lowest wealth quintile to 7.25% in the highest quintile (186).

1.3.1.1. ART in Kenya

The public health programme to distribute ART began in Kenya in 2003, but it was not until 2006, after a presidential declaration, that ART became free to the public and those eligible could access it in greater numbers (187). More recently, Kenya has increased domestic investment in HIV treatment and prevention, doubling HIV related spending from 2008 to 2010 (30). Despite this, more than 75% of funding for HIV programmes still comes from international sources, indicating continued reliance on international aid (30), which could be extremely problematic for Government and Kenyan PLWH should this aid be withdrawn at any time. Kenya is named as a target country in the Treatment 2015 programme (9), and the Kenyan Government has adopted the suggested target of 90% coverage by 2015 (182).

Currently in Kenya the recommendations for ART in adult patients are for first line therapy if their CD4 count is equal to or below 350 CD4 cells/mm³, at WHO stage 3 or 4, are co-infected with TB or Hepatitis virus with evidence of liver failure (46). First line treatment is Tenofovir, Lamivudine and Efavirenz or Nevirapine, or Zidovudine, Lamivudine and Efavirenz or Nevirapine. Second line therapies are given when first line therapy fails, and substitute the Nevirapine or Efavirenz for a Ritonavir boosted protease inhibitor (46). About 1% of urban Kenyans are currently accessing second line treatment (20).

Recent data from a retrospective cohort study in Zambia estimate mean costs of ART range from \$2.34 per month to \$36.7 per month, depending on the regimen (188). When costs beyond ART, such as co-trimoxazole or blood tests were entered into the calculation, mean monthly HIV treatment costs per patient was \$243 (95% CI, \$194-\$293), ranging from \$184 (95% CI, \$172-\$195) to \$304 (95% CI, \$290-\$319) depending on clinic site (188). This mean monthly treatment cost represents 21 323 Kenyan shillings at the time of writing, with Kenyan a minimum wage for unskilled labour of 5,218 per month (189). This highlights the Kenyan reliance on internationally supported programmes which enable subsidised or free ART.

Stavudine, which was previously included in all lines of treatment due to its high efficacy and low cost, has been phased out as per 2010 WHO guidelines because of the associated excessive toxicities. Fixed dose combinations are used when available to decrease pill burden and make adherence easier, but are often more expensive (183).

1.3.2. Mental health and well-being in traditional cultures

Although society is changing in many areas of Africa due to globalisation and industrialisation, it would be wrong to imagine that traditional beliefs concerning health and well-being have changed or been forgotten (190). Traditional beliefs, although differently expressed in different places, are maintained at a deep level for many people, whilst changes due to globalisation affect the visible or more material aspects of life (190).

Both disease and misfortune are seen as spiritual experiences in much of Africa, and therefore both are prevented and cured by the same practitioner – the medicine man (191). Treatment is determined by suspected cause, with rational treatments for natural ailments, and a combination of supernatural and rational treatment for supernatural ailments (191). The medicine man administers physical or spiritual (or psychological) treatment in the form of rituals or medicines made from plants, herbs, powders, roots, seeds, etc. Treatment often involves a lot of time and personal attention, which develops trust and understanding between the patient and the medicine man (190). Lambo, a Nigerian psychiatrist, describes how many African traditions understand mental ill health, and HIV infection itself to be as a result of natural, supernatural or spiritual factors (191). This understanding is based on a non-Western understanding of ‘reality’: in the western world, reality is concerned with things and mastery of things, whereas in traditional African culture where it is concerned with relations between people and other people and between all people and spirits (191).

As a result of these differences in understanding about health and illness, interventions which are effective in a western environment may not be as well received, or as effective when delivered in a more traditional culture. Fernando summarises how positive well-being in traditional African cultures includes a sense of unity in the spiritual and material worlds, combining empirical detail with elements of magic or fantasy (191). The differences between understandings of positive well-being in traditional African and Western cultures highlight the different basis on which each culture builds their understanding of ‘healing’ and ‘cure’, which may undermine the effectiveness of a culturally untranslated intervention.

1.4. Models of care for PLWH

1.4.1. Challenges with current models of care in SSA

Clinics in SSA are often over burdened, attempting to provide high quality holistic care, with increasing clinical responsibility for increasing patient numbers in under-resourced settings (192). A

retrospective cohort study from Kibera in Nairobi, Kenya found that 29% of patients dropped out of ART programmes for more than 90 days (20). The authors suggest this could be the result of the recent scale up of ART provision by 300% over 2 years, which has led to increasing patient numbers, increasing complexity of care and decreased available workspace (20). The increased pressures on healthcare systems due to the ART scale up are also evidenced in data from the WHO, which reports that 38% of countries (50% in SSA) reported ART stock-outs in 2010 (193). This lack of consistently available ART is an indication of the serious threat to scale up success, and highlights the precarious nature of healthcare system capacity.

1.4.1.1. Mental health as a area of neglect

High patient burden also places pressure on clinics trying to comply with ART guidelines in Kenya, which recommend counselling and psychosocial support for all, in addition to a programme called prevention with positives, which covers sexual health and family planning (46). Currently, the care offered to PLWH as described in section 1.1.3, is focused on viral control with referral to psychological or social support when problems are detected, often through a drop in medication adherence (47).

In Kenya, this also reflects the training of healthcare professionals providing the care, most often nursing staff, which has a medical focus. Undergraduate nursing students at the University of Nairobi, for example, are well trained in history taking, physical examinations, and health maintenance, but not in the importance of holistic care, communication skills, negotiating decision making or compassionate care (194). It is unknown why this emphasis on medical skills exists. It is possible that this is a remnant from when nurses as a profession first worked in Kenya and other colonies, exporting the colonial era understanding of well-being using the biomedical model of medicine, with an emphasis on physical well-being, and the role of nurses being the assistant to the medical profession. Nursing has developed as a profession, mostly since the development of the first nursing theories since Florence Nightingale, with Peplau's model of interpersonal relations, which widened the focus of nursing care to nursing to patient centre care and the holistic approach (195). There is evidence that a patient centred approach is preferable for patients and is effective in increasing patient satisfaction and symptom burden (196)

This focus on the medical and physical aspects of well-being, at the expense of a holistic view of health, places the mental health and well-being of patients under threat. This is particularly relevant when there are external pressures to focus solely on medical aspects of care such as ART provision. The excessive pressure and demands made on healthcare professionals in the delivery of care also

decrease the likelihood that the required resources for holistic patient centred care are made available.

This has been recognised by the UK Consortium of AIDS and International Development (UCAID), who designed the HIV Care and Support Initiative, which identifies a global problem of psychological and social care as the “forgotten pillar” of the HIV response (48). UCAID designed a road map, which charts the progress towards universal access to care and support by 2015 and contains guiding principles for care and support (197). It has also conducted a mapping exercise looking at the global response to the epidemic in terms of care and support in 2013. It describes the emergence of a new direction in strategy documents of agencies responsible for the coordination of the international response to HIV, such as WHO, UNAIDS and the World Bank (198). The focus of the response has begun to shift from emergency response towards the chronic management of HIV, responding to the wider needs of PLWH and their communities, strengthening social protection and streamlining care with the management of other chronic diseases and child and maternity services. This is a hopeful message in the context of Treatment 2015, which through increasing pressure on governments to focus on numbers of people on ART and numbers of AIDS related deaths, risks local decreases in financial and political support for the psychological and social care of PLWH in resource poor settings. It is unclear however, what this shift might look like in different country contexts, and whether it is radical enough to address the unmet need currently experienced by PLWH.

The identified burden of psychological and social problems reported by PLWH, demands a more concerted, holistic approach to care, and further academic study of its effectiveness for PLWH at the individual level and at the level of healthcare systems in countries such as Kenya.

1.4.2. Holistic care

First described by the South African philosopher statesman and prime minister Jans Smuts, holism is defined as the concept that living organisms are unified and indivisible, made up of parts which are both interdependent and interrelated (199). Holism is often viewed as synonymous with the Biopsychosocial model of care, developed by Engel (200). Engel argued that the pre-existing biomedical model was no longer relevant or useful for the tasks and social responsibility of medicine or psychiatry, and that it employed a mind-body dualism which disregarded the social, psychological and behavioural aspects of illness (201). His extended model of holistic care is also in line with the WHO definition of health, which highlights the importance and interdependence of well-being in physical, social, psychological and spiritual domains (53). An early study of the effect of holistic care

on patient outcomes found that the holistic approach improved patient mood, positive evaluation of care, and patient relatives' views of medical personnel (202).

1.4.2.1. Holism in chronic illness

Patients with chronic conditions such as PLWH on ART or cancer, no longer face a predictably short life span, but continue to need extra support for themselves and their families, beyond what would be required in less complex or stigmatising medical conditions (203). In cancer care, supportive care has been developed to meet the extra needs associated with the diagnosis of a chronic and potentially life-limiting condition. Supportive care is defined by a recent systematic literature review and Delphi study as:

'The multi-disciplinary holistic care of patients with malignant and non-malignant chronic diseases and serious illness, and those that matter to them, to ensure the best possible quality of life. It extends as a right and necessity for all patients, is available throughout the course of the condition, concurrent to condition management and is given equal priority alongside diagnosis and treatment. It should be individualised, taking into account the patient's past life experiences, their current situation and personal goals.' (204).

This definition of supportive care includes multidimensional symptom control, supported decision making, increased patient professional communication and empowerment of the patient and their family in the self management of their condition (204). Supportive care has links with and sometimes involves palliative care, as an approach to care which seeks to improve quality of life for patients and the families of patients with life limiting conditions, through multidimensional symptom control.

In the context of care for PLWH in Kenya, supportive care in line with the recognised international definition is not adequately accessible for PLWH (204, 205). This kind of care is more often provided informally by the community and family, but because of the stigmatising nature of HIV, or because the family itself is also in need of support, this does not always occur (198, 206). When supportive care such as multidimensional symptom control and holistic person centred care is provided in Kenya, it is usually within the remit of palliative care (207).

Regional and local bodies promoting palliative care within Kenya, and linking in with other palliative care associations in the region, have made much progress in the promotion of holistic, person-centered care for people in the final stages of disease and at end of life (23). The palliative care movement in Kenya is growing, increasing number of professionals with skills and knowledge in the management of multidimensional symptoms (207). These professionals have much to offer PLWH,

particularly in terms of symptom control, patient centred care and patient education (9, 48). Kenya was recently categorized as a 4a country by the International Observatory on End of Life Care, which means that palliative services in Kenya are at a stage of preliminary integration into mainstream service provision (26). This specialism could prove a potentially viable source of high quality holistic care for these patients, which is currently not available.

1.4.3. Palliative care approach as holistic care

The WHO defined palliative care in 1992 as:

‘an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual’(59).

In Kenya, healthcare professionals providing palliative care are supported by the Kenyan Hospice and Palliative Care Association (KEHPCA), which has a mandate for advocacy, training and public education. KEHPCA runs a regular training programme for physicians, nurses and allied health professionals to increase the body of knowledge regarding palliative care among generalist healthcare professionals and to increase the number of specialist practitioners in the country (207). KEHPCA works in close collaboration with the African Palliative Care Association (APCA), developing guidelines and standards, validating research tools for audit and quality control and promoting quality palliative care for all in need (23, 49, 208).

1.4.4. HIV and palliative care

Before the advent of widespread access to effective ART, palliative care was the mainstay of HIV care in the absence of curative treatment options (209). Before the widespread availability of ART, in 2000, it was advocated as a public health approach by UNAIDS (210). In resource poor settings, it was delivered through community members who were mobilised to care for the increasing burden of sick and infirm AIDS patients (211). Evidence for the effectiveness of palliative care interventions in LMIC is sparse (212), however, holistic, supportive care models of HIV care which could be described as delivering care using the approach of palliative care do currently exist (213). They receive relatively little attention and are mostly small scale and organised at a community level, often relying on minimally trained community based volunteers (211, 214). Since the advent of increased access to ART, with the associated reduction in physical morbidity and mortality,

international interest and financial support has shifted to the push to improve access to life prolonging treatment (1, 9, 30, 215).

1.5. Evidence for the effectiveness of palliative care interventions for positive mental health and well-being

Palliative care guidelines recommend that care focus on physician-patient communication, assessment and treatment of pain and other symptoms, psychological, social and spiritual support and co-ordination of care (59, 216, 217). However, within these guidelines, as palliative care is a patient centred intervention, the components of a consultation vary widely depending on patient need. In order to evaluate the evidence for the effectiveness of palliative care in promoting mental health and well-being, it is necessary to first describe the common components of a palliative care consultation.

A recent analysis of data collected as part of a wider randomised trial of palliative care in lung cancer patients in the US documented that a palliative care consultation in the outpatient setting took a mean of 59.5 minutes (sd 28.6) (218). This was divided between symptom management (25.7 minutes (sd 15.8)), patient and family coping (19.6 minutes (sd 14.7)), and illness understanding and education (10.4 minutes (sd 7.6)) (218). A phase II RCT of palliative care for lung cancer patients in the US, described palliative care delivered to their participants as a full medical, physical and psychosocial assessment, which led to recommendations for support in symptom control, education, counselling and home care (219). These components can be summarised as symptom control, counselling and support and education and understanding. The evidence for these interventions on mental health and well-being is summarised below, first for similar chronically ill patient populations (cancer, asthma, mental health, stroke, diabetes and chronic heart failure), and then for PLWH (Table 1-5).

Table 1-5 Evidence of the effectiveness for components of palliative care and whole palliative care packages on mental health and well-being of patients with chronic conditions and for PLWH

Component of palliative care	Evidence of effectiveness on mental health and well-being	
	From the non-HIV literature (Cancer, asthma, mental health, stroke, diabetes, heart failure, COPD)	From the HIV literature
Symptom management	<ul style="list-style-type: none"> Decrease in asthma symptoms due to self management intervention associated with decrease in depression (220) Improvement in physical symptoms management in COPD through pulmonary rehabilitation associated with decreases in depression and anxiety (221) 	<ul style="list-style-type: none"> No evidence for effectiveness of an intervention identified but copious evidence of unaddressed physical symptoms alongside psychological distress (11, 12, 222-224)
Patient and family support psychological, social or spiritual	<ul style="list-style-type: none"> 40 seconds of physician compassion reduced anxiety in breast cancer patients (225) Counselling by minimally trained counsellors more effective than usual care for depression and anxiety in anxious or depressed women in Pakistan (226) 	<ul style="list-style-type: none"> Community led health support associated with increased social support and decreased stigma in PLWH in Ethiopia (211) Informal phone support groups improved self efficacy, help seeking and decreased social isolation for PLWH (227) Participation in online support groups associated with improved mental health and well-being (228) Interpersonal therapy for PLWH found reduced depression in intervention group in South Africa (229) Group educational and psychological support effective in decreasing anxiety, depression and perceived stress (230)

Component of palliative care	Evidence of effectiveness on mental health and well-being	
	From the non-HIV literature (Cancer, asthma, mental health, stroke, diabetes, heart failure, COPD)	From the HIV literature
Illness understanding and patient education	<ul style="list-style-type: none"> • Cochrane review identifies decrease in depression associated with increased patient education in stroke patients (231) • Advanced cancer patients reported decrease in depression with a nurse led psycho-educational intervention in USA (232) • Patients with life limiting illness reported decrease in depression and increase in spiritual well-being, through adult affective educational support programme in USA (233) • Systematic review identified improvements in psychological well-being in diabetic patients due to educational intervention (234) 	<ul style="list-style-type: none"> • Systematic review identified evidence for effectiveness of information, counselling, and testimonials for reducing HIV related stigma (235) • Emotional symptom self-care intervention reduced depression, anxiety and stigma in African American women (236) • Group educational and psychological support effective in decreasing anxiety, depression and perceived stress (230)
Palliative care	<ul style="list-style-type: none"> • Cancer, heart failure and COPD patients in USA, reported decrease in anxiety through advance care planning, psychosocial support, and family caregiver training (237) • Patients diagnosed with lung cancer reported decreased depression and improved quality of life compared to control (238) • Systematic review identified palliative care decreased anxiety in cancer patients (239) 	<ul style="list-style-type: none"> • Systematic review identified palliative care decreased in anxiety in HIV patients in UK and USA (review) (212) • Palliative care for PLWH associated with improved psychological quality of life in Tanzania (240)

The evidence summarised in Table 1-5 describes the effect of relieving physical symptoms on mental health and well-being in patients with COPD and asthma, and highlights the lack of evidence in PLWH populations, despite numerous studies identifying evidence of unaddressed physical and psychological symptoms. There is evidence that providing psychological, social or spiritual support relieves psychological distress in breast cancer and mentally ill patients, in addition to PLWH.

Evidence for the effect of increasing illness understanding and patient education on psychological distress is strong in patients who have experienced stroke, cancer, diabetes and life limiting illness. In PLWH it has been found to reduce stigma, depression, anxiety and stress.

This evidence suggests that a palliative care approach, with focus on holistic and patient centred care and the Biopsychosocial model of well-being is a plausible solution to the multidimensional problems reported by PLWH.

1.6. Summary

This chapter has discussed the epidemiology of HIV, recent advances in HIV care, concepts of mental health and well-being, and the changing healthcare needs of PLWH from acute management to chronic care.

Due to the changes in eligibility for ART, the population of PLWH on ART will continue to grow, to 15 million people at least by 2015. This patient population experience increased prevalence of depression and anxiety compared to the general population, in addition to the social stigma of HIV. This adversely affects their quality of life, and also impacts on the potential effectiveness of the international ART roll-out. International bodies continue to exert pressure on domestic governments to reach ambitious targets for increasing access to ART, in the difficult context of the global financial crisis, decreased access to international funding and increasing patient numbers.

Supportive, holistic, patient centred care for PLWH, which is culturally appropriate and accessible to all who are in need, is suggested as a solution to this growing complex problem, particularly in this political, economic and epidemiological context. Palliative care is a growing movement in SSA, with increasing numbers of locally trained professionals, guidelines and clinical outcome measures. Therefore palliative care offers a plausible solution; particularly as holistic care is not delivered elsewhere in healthcare. Palliative care integrates care holistic care with the pre-existing expert bio-medically focused disease management, drawing on the local skills and expertise of Kenyan palliative care professionals.

2. Aims and objectives

2.1. Aim

To evaluate the effectiveness of a nurse-led palliative care intervention on the mental well-being of HIV patients on ART in Kenya, and to explore active ingredients of the intervention and their mechanism of action and therapeutic aspects of participation

2.2. Objectives

1. To determine baseline levels of mental well-being and to examine associations between baseline mental well-being and demographic and clinical characteristics among patients with HIV on ART enrolled in a randomised controlled trial (RCT) of a nurse-led palliative care intervention.
2. To identify any effect of the palliative care intervention on mental health and well-being, comparing the intervention with standard best practice.

This objective contains one null hypothesis:

There will be no difference in psychological quality of life, measured by the MOS-HIV MHSS, in longitudinal analysis of difference between participants allocated to receive the intervention (nurse led HIV palliative care) and participants allocated to receive the control (standard HIV clinic care).

3. To determine and describe participant experience and longitudinal response to participation in the study in terms of mental health and well-being, and to identify and explore associations between participant response and demographic and clinical characteristics.
4. To identify and explore the existence of “active ingredients” and mechanisms of action of the intervention and therapeutic aspects and processes of study participation.

3. Methods 1: Study design, rationale and methodological considerations

3.1. Introduction

This is a mixed methods study evaluating the effectiveness of a nurse-led palliative care intervention on mental health and wellbeing in HIV positive patients on ART. In this chapter I describe and justify the study design and choice of methods for this study, exploring methodological considerations relating to conducting research using both quantitative and qualitative approaches.

3.2. The study context: the TOPCare study

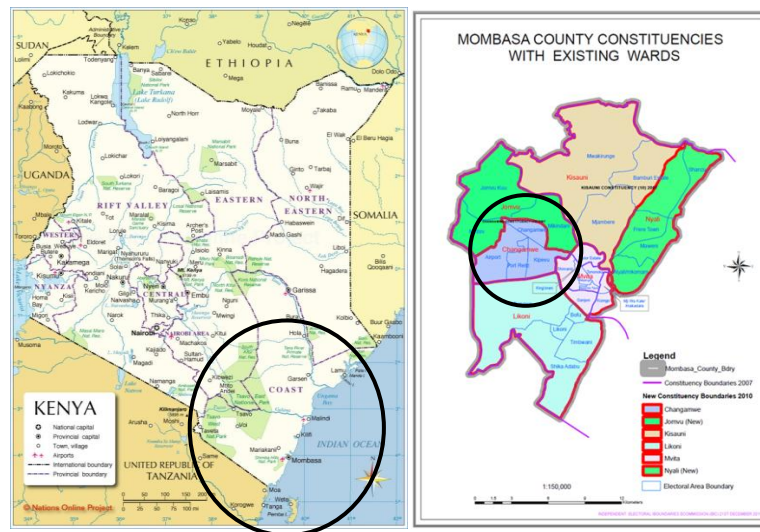
This thesis was conducted as part of the TOPCare study, which is an RCT assessing the effect of receiving palliative care delivered by nurses experienced in the delivery of ART and trained in palliative care, on participant reported outcomes such as pain, symptoms and mental morbidity (ClinicalTrials.gov Identifier: NCT01608802). The primary outcome tested by the TOPCare study was the effect of the nurse-led palliative care on patient reported pain and symptoms (241). This thesis focuses on the psychological and social outcomes, which were the secondary outcomes of the TOPCare study. Patients who were adult, HIV positive, on ART for more than one month and reported pain or symptoms of 3 or more on the APCA African POS (APOS) (0-5 scale) were eligible for inclusion. The protocol for this trial was published in the peer reviewed journal, BMC Infectious Diseases and is available in Appendix 5.

3.2.1. The study site

The study site, Bomu Hospital, is in Mombasa, the second largest city of Kenya, located in the Coast region. The hospital is within a constituency of Mombasa called Chamgamwe, which is on the Kenyan mainland (rather than Mombasa island), accessible to Mombasa island by the Makupa causeway (Figure 8). Chamgamwe is an industrial area with an oil refinery and a port. Residents of this area are mostly labourers in the refinery, the port or the nearby airport. The province of Coast is bordered by Tanzania to the south and the Indian Ocean to the east.

Methods 1: Study design, rationale and methodological considerations

Figure 8 Map of Kenya, highlighting the Coast region, and map of Mombasa with Chamgamwe indicated



The 2009 census reported a population in Chamgamwe of 69 251 people, contributing to a total of 523,183 people in Mombasa, and 38 610 097 people in Kenya (186). Forty-six percent of Mombasa residents have piped water (compared with 30% overall in Kenya and 75.7% in Nairobi), 5.8% are connected to the mains sewers (8% in Kenya, 48% Nairobi) and 65% of households have access to a mobile phone (63% in Kenya, 88% in Nairobi) (186).

Some images from Chamgamwe and Bomu Hospital can be found in Figure 9 and Figure 10.

Figure 9 Chamgamwe



Figure 10 The registration room in the clinic where patients are registered and Dr Aabid Ahmed the executive director showing Dr Richard Harding around the hospital in December 2012



Bomu Hospital is the flagship institution of the Mkomani Society, a philanthropic non-governmental organisation based in Mombasa. It has a catchment population of 3.3 million people and sees 300,000 patients annually. The society, founded in 1979 on philanthropic values, currently runs four clinics, of which three provide medical care (205). The Comprehensive Care Clinic (CCC) at Bomu hospital, which was our study site, has enrolled 28,000 HIV positive patients, of which 10,000 are on ART. The clinic provides care for about 400 patients daily. Details of the sources of funding and services provided at Bomu Hospital are described in Table 3-1.

Table 3-1 Description of services available at the study site, the CCC and within Bomu Hospital (184)

Sources of funding	Services provided
<ul style="list-style-type: none"> • Centre for Disease Control • US Agency for International Development (USAID) • US President's Emergency Plan for AIDS Relief (PEPFAR) • New York University • Project Sunshine • International Development Relief Fund • Kenyan Government - Ministry of Health 	<ul style="list-style-type: none"> • Volunteer HIV counselling and testing • Prevention of mother to child transmission of HIV • Maternal and child health • Community outreach • Diabetic clinic • Ear nose and throat clinic • Hypertension clinic • Surgical clinic • Gynaecology clinic • Paediatric clinic • Outpatient HIV clinic • TB clinic

The CCC, where patients were recruited into this study, is a busy HIV clinic, open from Monday to Friday (205). Care for HIV positive patients is provided free of charge, with a small fee for other

services such as surgical or maternity care. Basic essential HIV medications including ART and simple antibiotics are also free, but patients must pay for any medication outside of this list.

3.2.1.1. Patient processing

Upon arrival at the clinic patients are registered and self-select a waiting area, dependant on whether they are attending for an ART prescription refill and do not need medical attention, or have a complaint which they feel needs the attention of a medical officer. Those attending for ART refill are seen by one of seven triage nurses, who perform a brief screen to decide whether the patient has any problems which should be addressed by the medical officer, or can be managed by the nurse.

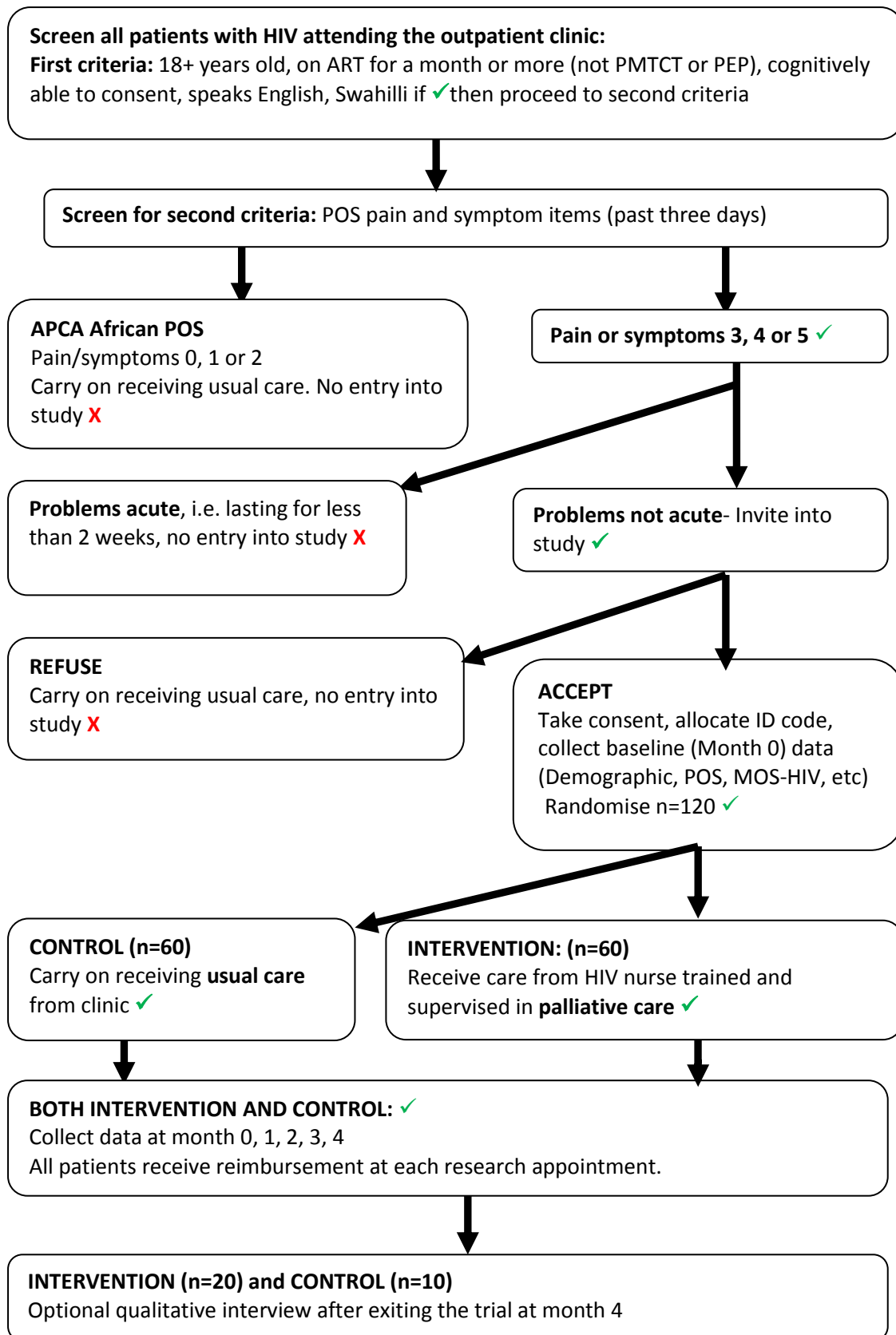
Once seen by a triage nurse or medical officer, patients receive their ART refill, and if appropriate are then referred for further support or investigations to relevant members of the multidisciplinary team such as clinical officers, nutritionist, family support workers and adherence counsellors. There is also a team of tracers who work in the community to ensure the clinic staff maintain contact with patients who have defaulted from care or are in need of further support and to facilitate adherence.

3.2.2. TOPCare study

3.2.2.1. TOPCare participant flow

Participant flow in the TOPCare study is described in Figure 11. Potential participants were screened through two sets of criteria to verify that (1) they were adult, on ART for more than a month (not PMTCT or PEP), were cognitively able to consent and spoke English or Swahili, and then (2) to screen for a score of 3, 4 or 5 for pain or symptoms on the APOS (scale 0-5) lasting more than two weeks. If potential participants subsequently agreed to participate, they were randomised to receive either standard care or the intervention care package.

Figure 11 TOPCare trial flow diagram



Methods 1: Study design, rationale and methodological considerations

The number of contacts with clinical and research staff for participants in the control and intervention study arms is depicted in Table 3-2. Intervention participants received a minimum of 7 contacts with the study nurses, compared with 4 with clinic staff for the control participants. Participants in both study arms were able to access healthcare when a problem arose outside of the scheduled contact points if necessary – patients in the intervention group arm with the study nurses and those in the control arm, with the clinic nurses. All participants in the study received five data collection appointments with the researcher.

Table 3-2 Chronology of appointments for data collection and delivery of the intervention.

	Data collection appointments for all participants	Minimum study nurse appointments for intervention	Minimum clinic nurse appointments for control
Baseline	✓	✓	✓
Within 1 week of first contact		✓	
Within 2 weeks of first contact		✓	
Month 1	✓	✓	✓
Month 2	✓	✓	✓
Month 3	✓	✓	✓
Month 4	✓	✓	✓

3.2.2.3. Data collection

The researcher administered the quantitative outcome measures at baseline and then monthly throughout the study period of five months. Researcher recruitment, training and data collection procedure is discussed in further detail in section 4.4. The outcome measures used in the TOPCare study were a demographic questionnaire, the APOS, Medical Outcomes Study for HIV (MOS-HIV), General Health Questionnaire (GHQ 12), Client Services Receipt Inventory (CSRI) and questions on adherence to ART and sexual risk taking. Examples of all measurement tools can be found in Appendix 6

3.2.2.4. The intervention care package

The intervention care package was delivered by two HIV specialist nurses from the standard care clinic, who received two weeks of palliative care practical training and ongoing clinical support. They used a clinical assessment tool to assess and plan care, and referred complex cases to the local

hospice for ongoing support. The minimum package of palliative care consisted of one visit within the first week following recruitment, one further visit within the second week, and then one visit per month for a minimum total of seven visits.

Training

The two nurses from the CCC who self-selected to participate in the study, each have many years experience in the clinic and were experts in ART care, adherence counselling and family planning.

The palliative care training they received consisted of five days didactic training followed by five days of practical experience in a palliative care setting. The training was provided by KEHPCA and included sessions on the principles of palliative care, mental health assessment and care, teamwork, pain assessment and management, spiritual and cultural issues, communication and counselling, sexuality, ethical and legal issues, self-care and stress management, breaking bad news, nutrition, symptom management, and the concepts of death, loss and bereavement. The nurses then spent five days shadowing staff at the local hospice, an institution with a multidisciplinary team which has been delivering palliative care in this region since 2001. The hospice routinely provides care for patients with life-limiting illnesses in the Mombasa region and offers out-patient services, home based care, hospital visits and day care. They aim to provide support and training for families of patients in home settings, where they can be more comfortable, and to promote training and development for health care professionals, workers and volunteers in palliative care in the Coast province.

Clinical supervision

Clinical supervision was provided by the co-ordinator of the hospice supporting the project to the nursing staff delivering palliative care. The co-ordinator of the hospice supported the staff from the point of training until the study closed. This established a relationship of trust and support which continued throughout the study. Initially, the clinical supervisor attended the study site twice a week to review all patient notes and offer solutions to problems the study nurses encountered during the course of delivering palliative care. In particular, in the initial stages when the nurses were still building their skill-base and confidence and when cases were especially complex, each clinical decision taken would be jointly reviewed and discussed by the clinical supervisor and the nurses, encouraging skill development and problem solving. The supervisor also encouraged the staff to be reflexive about the care, its impact on them in terms of stress and emotional burden and how they could manage this.

Complex cases

Clinical cases which the nursing team felt unable to tackle or which required medications that could not be dispensed at the clinic, such as strong opioids, were referred to the hospice for further management. Complex cases of pain or symptom management requiring specialist palliative care were also referred for co-management with hospice staff.

Clinical assessment

The clinical assessment sheet (Appendix 7) was designed as a prompt to ensure that participant assessment was holistic. Its design was informed by assessment sheets currently in use by palliative care providers across SSA, and cover physical assessment, including pain, symptoms and activities of daily living; mental well-being, including family, economic and emotional well-being; and spiritual well-being. The final element of the assessment sheet relates to ART adherence and potential side effects and toxicities. Every clinical assessment item was covered at every nurse-participant interaction, with a particular focus on the problems identified at previous sessions. To track participant progress during the trial the nurse completed a tick box summary at the end of the assessment to highlight areas of concern, which were then recorded in the ongoing record. The ongoing record was a summary document which facilitated progress-monitoring and ensure chronic problem follow up (Appendix 8). In particular it was used to document problems identified by the participant and nurse during assessment and the action plan decided upon and subsequently revised on participants' progress or deterioration.

Intervention care package

Intervention participants received the palliative care assessment and care a minimum of seven sessions with one of two study nurses over the four- month course of the study. In addition to this, participants received the same standard HIV care delivered by the clinic nurses to participants in the control group.

Further to the assessment described above, the study nurses employed a holistic patient centred approach according to the training they had received. They also facilitated couples counselling sessions as the need arose, or when requested by participants.

The control – standard care

Those participants allocated to the control group were seen by the CCC nurses and continued to receive standard HIV care in an identical way to the other patients in the clinic. Once a month they attended the palliative care department to complete the study questionnaires. In line with the CCC protocols, patients initially attend the clinic for ART repeat prescriptions every two months with

decreasing frequency once medically stable. Because patients participating in the study were experiencing pain and symptoms and their CD4 counts did not exhibit an increasing trend, they attended the clinic once a month, in line with CCC protocol.

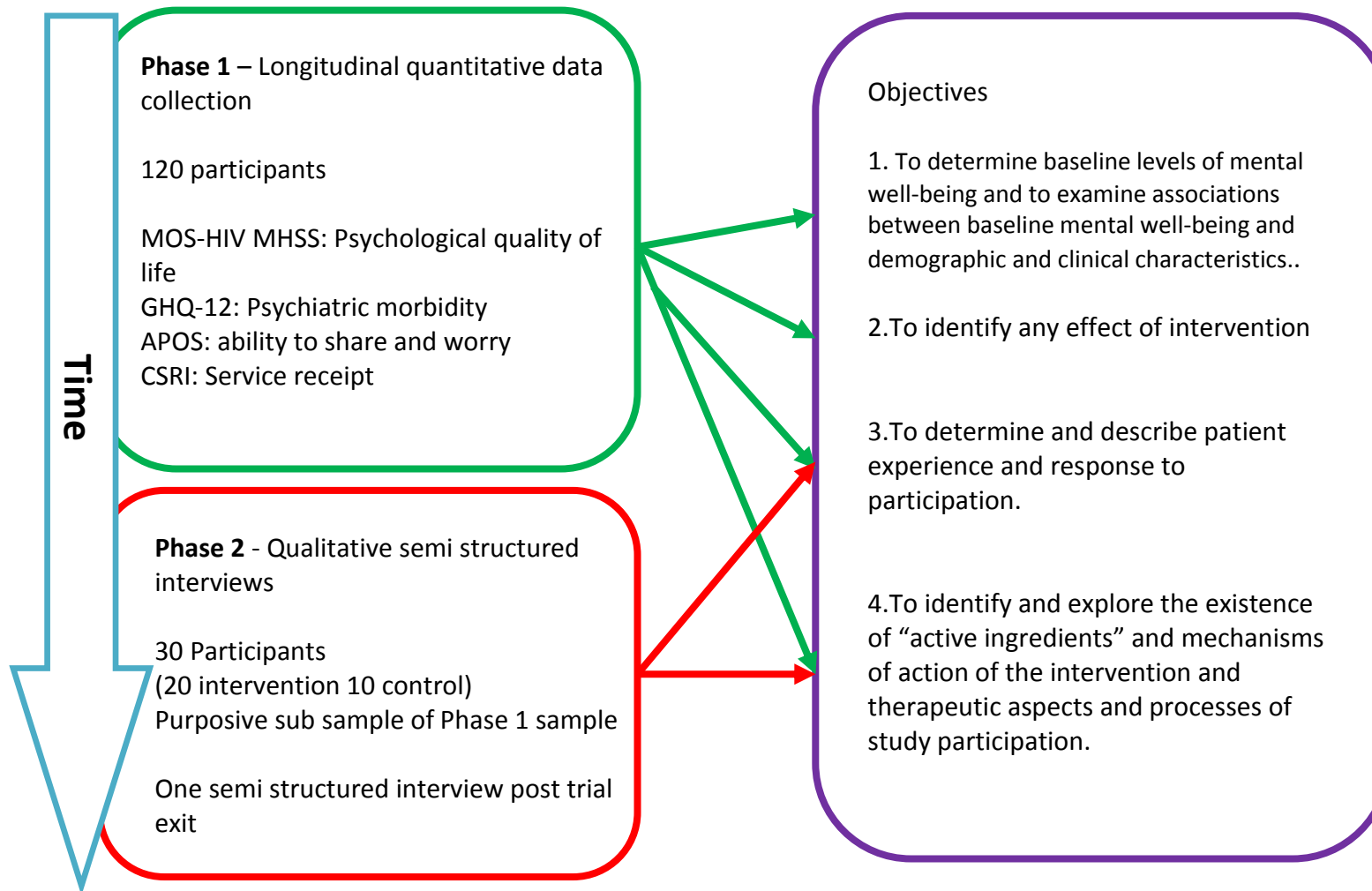
3.3. Thesis study design

This section will discuss the study design, the rationale for design decisions, provide a brief theoretical background of mixed methods research and discuss the methodological considerations for the study.

This thesis uses a mixed methods sequential study design (242, 243), with mixed methods providing an expansive function, in order to evaluate effectiveness of the intervention care package (the ‘what’), as well as reasons for any effectiveness (‘why’) in the context of participants’ experiences (‘whom’), (243, 244). The mixed methods design included a quantitative data (phase 1) and qualitative data (phase 2) collection phases, with the findings from the qualitative data expanding on the results from the quantitative data analysis. (245). Data integration occurred during the analysis, where the findings from the quantitative data were used to interrogate the qualitative data and draw meta-inferences (combined inferences from both types of data) and conclusions from both datasets. This adds richness and comprehensiveness to the study conclusions, and reflects the complexity of the intervention under study.

The thesis study design is depicted graphically in Figure 12. Phase 1 was composed of longitudinal quantitative data collection over a period of four months, followed by phase 2, for a sub sample of the TOPCare study that was purposively selected and consented to participate in one qualitative interview. Findings from analysis of data from each phase were used to address the objectives as illustrated in the map of the study design (Figure 12).

Figure 12 Map of thesis study design



3.3.1. Definitions of terms

This section contains definitions of terms used in the analysis and reporting of data for this thesis.

3.3.1.1. Active ingredient

Evaluation of multifaceted person-centred interventions can be challenging, particularly when compared to the evaluation of a discrete drug intervention, because of the difficulty in isolating the different aspects of the intervention that were effective (246, 247). This study adopts the concept of an active ingredient developed by the MRC, namely the specific aspect or aspects of a complex intervention which make it effective (247).

3.3.1.2. Mechanism of action

Closely linked to the concept of an active ingredient is that of the mechanism of action. This refers to the process or means through which an active ingredient exerts itself and interacts with other aspects of components of an intervention, the context and the participants, to produce an effect (247). Understanding this mechanism is useful in refining the intervention, for example by isolating or enhancing the mechanism of action of the most active ingredients in an intervention.

3.3.1.3. Mental health and well-being

The description and understanding of the concept of mental health or well-being developed by Walker *et al* will be used in this thesis to capture the intersectionality of the social, psychological and economic determinants of mental health (56). Their framework of the determinants of mental health is partially reproduced in Figure 3-6. The use of this framework rather than a simple definition of mental health, serves as an evidence-based reminder of the complexity and intersectionality of the concept.

Figure 13 Determinants of mental health or well-being (56)

Key determinants of mental health		
Social inclusion	Freedom from discrimination and violence	Economic participation
Supportive relationships Involvement in group activities Civic engagement	Valuing of diversity Physical security Self determination and control over one's life	Work Education Housing Money

3.3.2. Mixed methods research

This study evaluates the effectiveness of a nurse-led intervention on mental well-being, by quantifying and exploring changes in mental well-being throughout the study. Meeting the study objectives requires the use of mixed methods research, defined as combining qualitative and quantitative approaches into one study or a series of multi-phased studies (248), or the integration of both quantitative and qualitative data collection and analysis (243). The use of different types of data in the same study is increasingly common in research as it provides a more comprehensive account and more nuanced understanding, which is particularly important in the evaluation of complex interventions (247, 249). However, the use of qualitative and quantitative approaches within the same research design creates an epistemological tension, discussed below.

3.3.2.1. Evaluation of complex interventions

The intervention under study for this thesis is a complex intervention as defined by the Medical Research Council (MRC) (247). This means that it is context dependent and also made up of several interacting components, which themselves include measurable components and relatively un-measurable components; for example, 'nursing care' includes administering medications wound care, and as well as tacit and routine elements that impact on the difficult to measure concepts of 'quality' and 'compassion' (250).

RCTs are an important and powerful tool in establishing the efficiency of clinical interventions however, it is recognised that the use of traditional RCT designed is flawed, particularly for the evaluation of complex interventions to improve health (246). When evaluating the effectiveness of a simple intervention such as a medication, or a particular surgical technique, evaluation is focused on outcome. When the same approach is applied to a complex intervention this often generates inconclusive or confusing results, because mechanisms of effect may not be sufficiently clear and uncomplicated to produce a clear outcome (251).

In recognition of the importance of the complexities involved in evaluation, the MRC published guidelines for the evaluation of complex interventions in 2000 and revised guidelines in 2008 (246, 247). These guidelines specify that evaluation should include 5 steps. (1) preclinical, where theory is explored and hypotheses are chosen; (2) modelling, where the components of the intervention and underlying mechanisms which may predict effectiveness are identified; (3) exploratory trial, when constants and variable aspects of the intervention are described and a feasible protocol is developed; (4) definitive randomised controlled trial, where the intervention is compared with an

appropriate comparator, with defensible theoretical framework and adequate statistical power and (5) long-term implementation, where it is determined whether outcomes can be replicated in uncontrolled settings. Qualitative data collection and analysis is advocated in steps 1 and 2, to inform the exploratory and definitive trial, which will produce evidence of effectiveness (247).

Despite qualitative data input at the preclinical and modelling phases, if the underlying causal mechanisms of change differ from what was hypothesised and anticipated during these phases, there is a risk that a limited set of quantitative outcome measures might not be suitable to capture the effect of the intervention on their own (252). To anticipate this study's findings, a traditional RCT design using quantitative methods alone may have found that the intervention was ineffective, when in fact causation was more complex, involving the intervention's context and interactions between different intervention components (253).

Palliative care interventions are complex interventions because of the interacting components of the care package, the importance of context such as environment or disease, and also, because palliative care is patient centred, therefore components are delivered according to participant need creating many different combinations of treatment patients could receive (247). Because of this complexity, evaluations incorporating qualitative data collection and analysis are particularly suited to palliative care research, as this approach is better able to provide both breadth and depth of inquiry in addition to providing an understanding of complex causal mechanisms (27, 254, 255). It has been posited by some authors that this exploration of multiple causation and the effect of context would be possible with combinations of several RCTs such as multi arm or factorial RCT, calling this approach 'realist trials' (256). However, the extreme demand of this approach on the available resources in terms of expense and time made this option less feasible for this study. As a result, a mixed methods approach was selected, based on a critical realist philosophy.

3.3.2.2. Philosophical basis - Critical realism

Critical realism is a form of post-positivist philosophy, which posits that the world is complex and multidimensional, with many unobservable powers, structures and contexts which trigger reactions and responses in particular circumstances (257, 258). Initially developed by Baskhar, critical realism argues that it is essential to understand the underlying mechanisms of causation, which are sometimes expressed and visible or measurable, in tangible events or outcomes, but also may be hidden and unexpressed (259). Causation is understood to be complex, and mechanisms of causation are expected to vary under different circumstances and contexts, and are seen as 'tendencies' and not 'determinants' of outcomes (253).

Critical realism divides reality into three strata: the empirical, which is the expressed visible outcomes, and the actual, which is what occurs whether observed or not, and the real, where the causal mechanisms operate (259). For example, when looking at the sea, one might observe somebody surfing (strata of empirical reality). One may or may not observe the waves, depending on whether they break or not, but we know that they occur as they are necessary for surfing (strata of actual reality). The waves are in turn caused by the currents in the sea (strata of the real). In everyday life, causal mechanisms are more complex than portrayed in this example, and cannot be accurately described without contextual and supporting information which is not always available (for example, the ability of the surfer or weather). This leads most research to offer a partial explanation for causality at best (260, 261).

The unique contribution of critical realism to an understanding of social phenomena is to make the strata of their reality explicit, opening the possibility for their exploration (261). Critical realism emphasises that our social world operates in an open system, and that it is crucial for research to emphasise the essential role of social and environmental context in causation (262). (An open system is one which is vulnerable to context, where every element interacts with the environment and context and does not exist in isolation.) If researchers ignore these strata of reality and the complexity of causal or generative mechanisms, they would treat society, which is an open system, as a closed system, and increase the risk of making false assertions of causality (260).

Based on this theoretical understanding of how an intervention works, conclusions from critical realist research focus on causal mechanisms and context, and the way these relationships shape the outcome (258). This moves evaluation research, including evaluation of nursing interventions, from “what works?”, to “what works, for whom and why?”, affirming the contribution of both quantitative and qualitative data collection and analysis (262). In addition, without an understanding of the causal mechanisms, it is impossible to suggest reasons why an intervention is effective or not, and how any effect might have occurred (260). This is particularly important when evaluating an intervention which may be adapted for another context and refined to enhance effectiveness or efficiency (260).

3.3.2.3. **Methodology - Critical methodological pluralism**

Critical methodological pluralism is a critical realist paradigm for mixed methods (263). It is similar to pragmatism in welcoming a variety of methodological approaches and techniques, depending on the needs of the research question. However, in critical methodological pluralism the methods must also fit the ontological perspective (263) in this case critical realism.

It is commonly thought that an ontological tension arises when mixed methods are used to evaluate complex interventions. Qualitative methods often involve interpretivism and relativist assumptions, while quantitative approaches, are often based on assumptions of determinism and a successionist understanding of causality (253, 264). Previously, these approaches were in direct conflict, and were thought to be incompatible, (244, 265). This is resolved in critical realism. Because critical realism accepts the possibility of linear causality within a closed system, it is compatible with the model of an RCT. However, critical realism also accepts multiple causal mechanisms for an effect, and rejects the simplistic concept of direct cause and effect within a open system (253). As such critical realism is a sound ontological perspective for critical methodological pluralism.

Critical methodological pluralism emphasises the importance of using appropriate and if necessary different methodological approaches within the study design. Therefore, in order to evaluate this complex intervention, from a critical realist perspective, mixed methods have been chosen using the critical methodological pluralist paradigm, to gain breadth and depth of enquiry, and to understand the many causal mechanisms of action which may be occurring to create the outcome measured during this study.

To summarise, it is acknowledged that the traditional RCT design is inadequate to evaluate the complex interventions, such as palliative care. The addition of a qualitative component is recommended to increase understanding of context (246) and to increase the breadth and depth of inquiry (27). The use of qualitative approaches in conjunction with quantitative approaches introduces an ontological tension, which is relieved by adoption of a critical realist philosophical basis and a methodological paradigm of critical methodological pluralism. This enables the use of mixed methods to evaluate the complex intervention, with a clear ontological perspective.

3.3.2.4. Contribution of mixed methods

Mixed method evaluations of complex intervention focus on two key questions: firstly, is this intervention effective in everyday practice, and secondly, how does the intervention work, i.e. what are the 'active ingredients' or what aspects are key to effectiveness or to the change observed and how do they exert their effects (244, 247, 266)?

The aims and objectives of this thesis address both these questions (section 2, Pg 53). Specifically objectives 1, 2 and 3 address baseline levels of mental health and well-being and the evidence of effectiveness, and objective 4 addresses the existence of active ingredients and explores their mechanism of action, integrating mixed method data from both phases of the study (Figure 12).

The quantitative outcomes will contribute to an understanding of patterns or regularities in the sample, for example if mental health and well-being are associated with poverty or gender or education level (263). Without quantitative measures it is almost impossible to detect taxonomies, trends or patterns that warrant further investigation. Qualitative approaches become more useful when conducting an in depth study the patterns identified, or of respondents in specific circumstances, such as when describing the participant experience (objective 3) or identifying active ingredients for change (objective 4), or when underlying causal mechanisms are sought.

This evaluation was conducted cross-culturally. The literature strongly advocates that qualitative approaches to data collection and analysis be used in cross-cultural research, as it provides an opportunity for participants to express concepts which are important but may not be obviously relevant from the perspective on a cultural outsider (267). Qualitative approaches enable respondents to articulate their understanding of a topic from their own perspective, and not need to constrict and adapt their understanding to a framework devised by the cultural outsider (268).

3.3.3. Research questions by objective and rationale for methodology

3.3.3.1. Objective 1

To determine baseline levels of mental well-being and to examine associations between baseline mental well-being and demographic and clinical characteristics among patients with HIV on ART enrolled in a randomised controlled trial (RCT) of a nurse-led palliative care intervention.

The research question associated with this objective is:

What is the baseline level of mental well-being of the participants enrolled in the TOPCare study, before the intervention was delivered?

This objective will be addressed using the quantitative data from phase 1, to describe the outcomes from the MOS-HIV, the GHQ-12 and the APOS worry and ability to share items as measures of psychological quality of life, psychiatric morbidity and social well-being. This data will also be analysed for association with demographic and clinical characteristics.

3.3.3.2. Objective 2

To identify any effect of the palliative care intervention on mental health and well-being, comparing the intervention with standard best practice.

The research question for this objective is:

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Does receipt of the intervention affect the psychological quality of life, psychiatric morbidity, worry and the ability of participants to share their feelings?

Quantitative data from the MOS-HIV, GHQ-12 and the APOS worry and ability to share items will be analysed at monthly time points to identify differences between control and intervention participants. The data will also be analysed using longitudinal analysis techniques to account for data clustering by participant.

3.3.3.3. **Objective 3**

To determine and describe participant experience and longitudinal response to participation in the study in terms of mental health and well-being, and to identify and explore associations between participant response and demographic and clinical characteristics

The research questions for this objective are:

How and why do participants respond to participation in the study, and receipt of the intervention?

Is this response different in participants with different demographic or clinical characteristics?

Longitudinal summary measures (area under the curve) will be calculated for each participant from the phase 1 quantitative data, and will be analysed for association with demographic and clinical characteristics. Any associations identified will be used to interrogate the phase 2 qualitative data for patterns of response across demographic and clinical characteristics.

The qualitative data set will be analysed using thematic analysis with a focus on time, identifying descriptive themes to describe participant experience for both study arms before, during and after the study participation period. This will be reported in terms of participant experience of psychological symptoms and social experience.

This mixed methods approach will generate both process and outcome data to comprehensively address the objective.

3.3.3.4. **Objective 4**

To identify and explore the existence of “active ingredients” and mechanisms of action of the intervention and therapeutic aspects and processes of study participation

This is a mixed methods objective which will address the following research questions:

Methods 1: Study design, rationale and methodological considerations

What components of care were delivered as part of the intervention care package, and how did they differ from care received as in the standard care clinic?

Which aspects of the intervention and of study participation were associated with therapeutic benefit, and what were the processes of change?

To address this objective, data from the CSRI will be analysed to identify components of care delivered as part of the intervention care package, and compared with components delivered to those receiving standard care. The components of care provided as part of the intervention will then be analysed for association with area under the curve calculated to address objective 3 (longitudinal summative measure of well-being over time) to identify which components of care were associated with positive change in mental health and well-being.

Qualitative data from phase 2 of the study will be analysed to identify the active ingredients of the intervention and their mechanisms of action (from participants who received the intervention care package) and therapeutic aspects and processes of study participation (from all participants).

3.3.4. Methodological considerations

3.3.4.1. Thesis situated within a wider trial

Secondary outcome

It is important to remember that this thesis and research question use the secondary outcome of the TOPCare trial, the primary being change in pain score. It is reasonable to assume that if change in mental health and well-being was the primary outcome of TOPCare, the trial would have been designed differently. The statistical power of the sample was tested in the original study design to verify that there was adequate statistical power to detect a clinically significant change in the secondary outcome (MOS-HIV MHSS), but this will be rechecked for ensure statistical power for objective 2 of this thesis.

Generalisability

The sample for this thesis is taken from the TOPCare trial, which has inclusion criteria of moderate to overwhelming pain or symptoms, for two or more weeks, as measured by the APOS. Thus, the findings can only be generalised to this population, a HIV positive population, stable on ART, but with persistent pain or symptoms. To be classed as a stable ART patient means that the patient has been on the same regimen for some months, with decreasing trend in viral load and increasing CD4 count, and no unmanaged symptoms or opportunistic infections.

Methodological limitations due to embedded nature of qualitative component

Qualitative data collection conducted within a larger RCT risks having an auxiliary role, where the qualitative data is under conceptualised and added to the study design as an afterthought (264). This could be problematic if equal importance and thus attention was not attributed to data quality in each phase for both methodological approaches. Plano Clark *et al* suggest that tensions can be avoided when research questions and a protocol for mixed methods data collection, analysis and interpretation, are clearly defined from the start and both components of the study are thus given equal priority and consideration in the study design (264).

In this study, I carefully and fully developed the qualitative component as part of my thesis, but only after data collection for the wider the RCT had begun. However, qualitative data collection tools were designed with the same attention to detail and rigor as quantitative data collection tools, and the sample was selected purposively to address the objectives.

Further methodological limitations are discussed in the discussions section (Pg. 229)

3.3.4.2. Cross cultural and cross-language research issues

In the literature, cross-language and cross-cultural research is often critiqued for failing to recognise the impact of language on data quality, and underreporting steps taken to ensure cross-cultural or cross-language trustworthiness (269, 270). A recent systematic review identified failure to acknowledge role of translator, failure to pilot test interview schedule and failure to describe interpreter credentials as most prevalent unreported limitations (269). Additionally, when research is conducted in populations unfamiliar with research culture, concepts such as informed consent and even the concept of research (questions are asked with no expectation of response or action taken to address concerns raised) may be particularly concerning or confusing for participants (271). Concepts such as randomisation may not translate well, or may have cultural implications, for example associated with autonomy (271, 272).

Im *et al* developed criteria for ensuring that research was been conducted in a rigorous and respectful way, and to address some of the concerns identified above (273). They suggest the research topic must be culturally relevant, in that it must serve a need and improve the lives of participant members. Context must be considered, meaning that the social structural context of participants, and the ways in which this might influence their responses must be considered. Appropriate communication, conceptualisations and translations should be used and there must be mutual respect for all aspects of the researchers' and participants' cultures (273). Finally, the research must be flexible in terms of language and time taken for data collection.

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By using local experienced and qualified researchers who supported the local population to understand and engage with the research, we hope to have addressed these challenges and concerns. The researcher and research nurses acted as key informants, providing information and cultural translation for myself as the analyst in London (274). The qualitative data collection tools was piloted and subsequently amended and translators were selected based on their previous experience and on the quality of one interview transcript. A forum of regular communication and meetings and a culture of openness was set up to facilitate this role, so that the study team could openly feed back to the study design team whenever they felt there was an issue of cross cultural or cross language confusion. Further to this, to enhance transparency, all decisions and steps taken to increase cross language trustworthiness are reported in full in the analysis plan.

4. Methods 2: Protocol

4.1. Introduction

This chapter describes the study protocol detailing the procedures for data collection, sampling and recruitment. This is followed by a description of each quantitative outcome measure, sample size calculations for the primary quantitative outcome, and a detailed analysis plan for each objective.

4.2. Mixed methods matters

Issues of sampling, the process of data integration, management of conflicting findings and data quality specific to mixed methods research are considered within the design and implementation, to ensure quality inferences can be made (275).

4.2.1. Sampling

Rigorous sampling in mixed methods research combines the requirements of quantitative with qualitative approaches whilst maintaining the data quality of both components and therefore the quality of the meta-inferences of the study (276). As in all research, sampling in mixed methods research is determined by the research objectives, which also inform the sampling scheme (277). Quantitative probabilistic sampling is needed to generate findings which are generalisable to a population with similar characteristics (278). Qualitative sampling techniques purposively sample for generation of theory, to explore unique, typical or extreme cases or to achieve representativeness and transferability (276). There remains a tension between the focus of probabilistic sampling, which is to create breadth of information and the focus of qualitative sampling, which is depth of information on a smaller number of participants (278).

In this study, sequential mixed methods sampling was performed to resolve this tension (278). The sample for phase 2, the qualitative phase, is a sub-sample of the sample for phase 1, and was purposively selected based on study arm and response to the intervention in terms of MOS-HIV mental health summary score (MHSS).

The samples were also of adequate size to enable statistical power to detect change in quantitative data and to identify and explore different experiences of the intervention and participation in the study. This enabled the study to generate high quality findings from each phase and meta-inferences from all phases, to meet the study objectives (276).

The sample for phase 1 was chosen using probabilistic sampling from attendees at the clinic who met the inclusion and exclusion criteria. In total 120 participants were recruited based on the original TOPCare sample size calculations for the primary and secondary outcomes of the trial (241). From this, a sub sample of 30 participants was chosen purposively for the phase 2 qualitative data.

4.2.2. Data integration

In mixed methods research, findings from the analysis of each data type can be integrated at collection, analysis or interpretation (243). In this thesis the findings were integrated during all three stages.

Firstly, integration during data collection was conducted using the results from the analysis of the quantitative data to inform sampling for phase 2. MHSS was used to identify those who had responded to a clinically significant extent and those outliers or deviant cases who had responded in a different or counterintuitive way for inclusion in the sample for phase 2. This is discussed in further detail in section 4.4.2.1.

Secondly, findings from the quantitative data analysis were used to interrogate the qualitative data to meet objective 3 (see Figure 12). For example, and to anticipate, education was identified as associated with response to participation using quantitative analysis, and subsequently qualitative data on the participant experience were examined across levels of educational attainment (further details see section 4.6.5.2).

The findings from phase 1 contribute to addressing all objectives. The findings from phase 2 address objective 3 and 4.

Thirdly, interpretation in the form of meta-inferences drawn from the results of data analysis from both phases, were made (248).

4.2.3. Management of conflicting findings

It is not expected that the findings from each type of data will necessarily converge. Different methods and analytical approaches may produce data from the same sample which may converge, complement or diverge, particularly when the concepts under study are complex or multifaceted (279).

If conflicting findings from the analysis of data from phase 1 or 2 are identified, they were treated as fundamentally different, in that they provide different types of insight or perspective on the same complex intervention (252). By using a mixed methods approach, we increase the likelihood of

identifying divergent findings. This indicates an increase in the scope, detail and depth of an inquiry, viewing the same encounter from different angles and highlighting different facets or aspects of the complex phenomenon (279, 280). No data type or finding was privileged and all findings contributed to the meta-inferences of the study.

To ensure that any divergences were not due to a lack of data quality in any of the phases, a detailed and rigorous data collection and analysis protocols (outlined on pages 81, 86, 91 and 97) have been designed and followed (252).

The extent of divergence or convergence is sometimes used to indicate the external validity of findings, with convergence taken as strong evidence in favour of a finding, as a function of triangulation (279). Triangulation is not always assumed to act as an indicator of validity, but denotes simply that different methodological approaches have been used to study one phenomenon (281). Convergence of data from different sources could indicate shared bias rather than validity and therefore cannot be relied upon as a valid indicator of data quality (279). Particularly in sequential study designs it cannot be used to validate findings, because of the potential for the data collected first to bias the second (277). In this case the quantitative findings are being used to inform the qualitative interviews, and could affect the content of the interview. Therefore, whilst useful in exploring diversity of response and to gain a deeper understanding of the mechanism of action, triangulation will not be used as a measure of validity in this study.

4.2.4. Quality of mixed methods studies

While standards for measuring data quality are well established in qualitative and quantitative research methodology, standards in mixed methods are less well developed (282). However, O’Caithain *et al* have developed eight domains which will be used in this study to ensure the quality of the study design, data collection, analysis and inferences (283). This framework covers the quality of study planning, design, data, interpretation, transferability, reporting, synthesizability and utility. The framework is presented in Table 4-1 with details of its application and relevance for this thesis.

Table 4-1 Framework for data quality in mixed method research. Taken from O’Caithain *et al* (283)

Domain	Description	Application in this thesis
Domain 1: Planning quality	How well was the mixed methods aspect of the study planned?	Data collection tools, sampling strategy and analysis plans for both phases of the study were planned and developed specifically to provide the mixed methods data required to address the study objectives.
	Was there a strong rationale for the use of mixed	Mixed methods were required to evaluate the effectiveness of the intervention in terms of outcome and process, with qualitative data providing an expansive role.

Methods 2: Protocol

Domain	Description	Application in this thesis
	<p>methods?</p> <p>Is the execution time frame feasible?</p>	<p>Data collection, analysis, reporting and initial dissemination activities were planned to overlap, reducing waste of nurse and researcher time, and fitting all activities into the time frame required by the project grant.</p>
Domain 2: Design quality	<p>Is the design: Transparent?</p> <p>Fit for purpose?</p> <p>Strong?</p> <p>Rigorous?</p>	<p>The study has a sequential expansive design (243). A map of the study design is reported in Figure 12.</p> <p>Validated outcome measures are used to measure quantitative levels of mental health and well-being. Qualitative method are used to examine active ingredients and therapeutic aspects of participation.</p> <p>Methods chosen will provide breadth and depth of enquiry, and will be used to provide compensation for each others weaknesses in this regard.</p> <p>Methods chosen will provide quantitative data on the magnitude and frequency of constructs and qualitative data on the meaning and understanding of constructs (284)</p>
Domain 3: Data quality	<p>Is there: Data transparency?</p> <p>Data rigor/design fidelity?</p> <p>Sampling adequacy?</p> <p>Analytic adequacy?</p> <p>Analytic integration rigor?</p>	<p>There is a rigorous data collection and analysis plan detailing the choice of methods and rationale for these choices (sections 4.3, 4.4 and 4.6).</p> <p>The study has been designed to maintain data rigor despite the time and logistic constraints of a mixed method study design (Pg 62).</p> <p>Sample size calculations were performed to ensure adequacy for phase 1 (quantitative component). The phase 2 sample (qualitative component) of 30 participants, is considered adequate for data saturation (276, 285).</p> <p>Data analysis techniques for quantitative and qualitative data were chosen based on recommendations and guidance from the literature, to address the objectives and study aim (286-288).</p> <p>Analytic integration took place during the interrogation of the qualitative data by the quantitative findings to address objective 3. To address objective 4, both quantitative and qualitative data were used, integrated to identify the active ingredients of the intervention.</p>
Domain 4: Interpretive rigor	<p>Is there: Interpretive transparency and consistency</p> <p>Theoretical</p>	<p>All findings were substantiated using the results of statistical analyses or text extracts from the qualitative interview transcripts. All statistical tests were tested for the violation of assumptions, and the results reported for transparency</p> <p>In the discussion, inferences were discussed within the context</p>

Methods 2: Protocol

Domain	Description	Application in this thesis
	consistency	of wider evidence. Areas of divergence were explored more fully to understand the mechanism and extent of trustworthiness and reliability of the findings.
	Interpretive agreement	The analysis process was constantly verified with my thesis supervisors, and will be published in the wider literature to ensure that any interpretations of the findings do not reply solely on myself (the researcher) and the research team.
	Interpretive distinctiveness	The credibility of interpretations was strengthened through the use of deviant case analysis which explored the possibility of other interpretations of the findings.
	Interpretive efficacy	Meta-inferences, were made whenever possible using both data sources when meeting objectives 3 and 4, without preference for either data type.
	Interpretive bias reduction	Data divergences are openly explored (section 4.2.3.)
	Interpretive correspondence	Findings and inferences are reported by study objective to ensure interpretive correspondence
Domain 5: Inference transferability (external validity or transferability)	Is there: Ecological transferability Population transferability Temporal transferability Theoretical transferability	<p>The inferences will be transferable to populations of similar setting and context – HIV patients on ART reporting moderate to overwhelming pain or symptoms.</p> <p>The extent to which the inferences are transferable to other populations or disease groups is unclear, because the multidimensional and highly stigmatising nature of HIV infection means that differences in the effect of social context might be a barrier to ecological transferability.</p> <p>This population of HIV infected individuals was stable on ART and therefore reflects the majority of HIV positive people in the world in the near future, in accordance with the international progress of ART roll out (30). Therefore there is good temporal transferability.</p> <p>The theoretical underpinning of the effectiveness of palliative care in caring for patients' mental health and well-being needs is explained in section 1.5.</p> <p>Thick description of the sample, context and intervention will provide evidence for transferability of the findings.</p>
Domain 6: Reporting quality	Report availability	The protocol of the TOPCare study is published in an open access journal online to promote transparency and research quality. The findings of the study will be adapted for and made available to patient groups, clinicians, members of the public and policy makers through a variety of means such as blog posts, articles in newsletters, professional interest body

Domain	Description	Application in this thesis
	Report transparency Yield	websites and alerts on social media. The trial is reported in accordance with the CONSORT guidelines (289), will be submitted to publication in peer-reviewed journals, regardless of whether a positive result is found, for academic integrity. The knowledge generated by this study reflects the mixed method approach, producing more evidence than two separate single method studies, due to the integration of data and meta-inferences this produces.
Domain 7: Synthesiability	Of sufficient quality for inclusion in systematic reviews	Use of well validated outcome measures, reported clearly and transparently, increases the possibility that this data can be used in systematic review, to consolidate and develop the body of knowledge surrounding the mental health and well-being of PLWH on ART. Data collection, analysis and reporting is of high quality and conducted in accordance with international standards (CONSORT)
Domain 8: Utility	Findings are used by clinicians and policy makers	Each finding and meta-inference from the study is associated with a recommendation for research, policy or practice to facilitate the dissemination process

4.3. Preparation for data collection

4.3.1. Selection, training and supervision of the researcher

The field researcher who performed the data collection for this study is a Kenyan national from Nairobi. She has considerable training and experience in conducting both quantitative and qualitative research to a high standard, and has been trained in researcher skills by staff from King's College London (KCL) for previous projects. She has worked in the field of palliative care research since 2007 (5 years in 2011 when data was collected). Before data collection began, she completed a two-day training course, run by myself and a colleague from KCL. Topics included are detailed in Table 4-2.

Table 4-2 Training content for TOPCare researcher

Topic
Background to the TOPCare study
Background and rationale for study
Aims and objectives
Timeline
Study procedures : Screening of participants; Recruitment; Consent; Booking appointments; Distress protocol; Randomisation
Ethics : Confidentiality; Data management and storage
Measurement tools: APOS; MOS-HIV; GHQ-12; CSRI
Routine reporting to KCL during the study : Reporting progress ; Importance of recording daily activity; Record keeping and data management
Data entry: Use of data entry programme; Importance of accuracy and attention to detail

During training, the researcher rehearsed data collection using the measurement tools in a mock interview, and had the experience of being asked the questions, to encourage reflective practice. She was also trained in interview techniques such as minimising bias when asking questions and was instructed and supported to maintain a professional demeanour.

4.4. Data collection, management and entry

As depicted in Table 4-3, data were collected from participants over a four month period through five data collection appointments.

Table 4-3 Time points for data collection during the study

Standard care participants	Baseline	t1	t2	t3	t4	Post study exit (Sub sample of 10)
Longitudinal quantitative data	✓	✓	✓	✓	✓	
Semi structured interviews (sub sample)						✓
Intervention care package participants	Baseline	t1	t2	t3	t4	Post study exit (Sub sample of 20)
Longitudinal quantitative data	✓	✓	✓	✓	✓	
Semi structured interviews (sub sample)						✓

The intervention participants also had clinical appointments with the nursing staff at these contacts, the frequency of which is graphically depicted in Table 3-2 on page 59.

4.4.1. Phase 1: Longitudinal quantitative data

4.4.1.1. Sampling and recruitment

Details of the sampling and recruitment for the quantitative phase of data collection are also provided in the published TOPCare study protocol (290).

Participants were registered at the Bomu Hospital comprehensive care unit (CCC) and consecutively screened. The researcher visited the clinic daily at different times to recruit participants. This was to ensure that if patients attending the clinic were different at different times or days (i.e. attending market or attending before or after work) they would have equal opportunity to be randomly selected for inclusion. To begin screening, she used a random number table to select a number which corresponded with a participant on the register of participants currently in the clinic. From this start point, participants were then screened consecutively for inclusion eligibility. The first set of inclusion criteria was that patients were adult and HIV positive. On finding a patient who met these criteria, she would apply the second stage of inclusion criteria and enquire whether they had been on ART for more than a month. This was to exclude patients reporting symptoms common in the initial months of ART, due to side effects, toxicity or immune reconstitution inflammatory syndrome (291). If patients had taken ART for more than one month, they were asked to rate their pain and symptoms on the APOS. If they reported a pain or symptom severity score of 3, 4 or 5 from a possible score of 0-5 (with 5 being the worst case) for more than two weeks, (to exclude acute cases unsuitable for palliative care) they were taken through the consent process and information sheet to ascertain whether they would be interested in participating in the study.

Randomisation

Participants consented completed a baseline data collection interview with the researcher, were randomised to a study arm: to receive either the intervention care package or standard care (control). Allocation to study arm was conducted by block randomisation. In practice the researcher had three pots, each containing 40 slips of paper. In each pot 20 slips were marked with an 'I' for intervention, and 20 with 'C' for control. The participant blindly selected a piece of paper from a pot. Each slip was discarded it after it had been selected. Only one pot was used at a time. Block randomisation ensured that the workload of the study nurses was manageable by limiting the amount of participants allocated to the intervention at any one time.

It was planned that the researcher would recruit five participants each week, therefore 6 months was planned for recruitment to be completed. Participants were replaced if one dropped out of the study after providing only one data point. Replacement participants were allocated to the study arm of the participant who prematurely left the study, and therefore were not entered into the randomisation process.

4.4.1.2. Data collection

Data collection was performed at monthly intervals by the researcher. Each participant was allocated a participant pack, stored securely in the palliative care department. Within the participant pack, each month was represented with a different coloured section to facilitate data collection and progress monitoring. Each section contained the specific outcome measures to be completed, as not all were used at each appointment. Participants were free to choose whether they conducted the interviews in English or Kiswahili or a mixture of both to ensure complete ease of understanding. Participants who did not attend an appointment were contacted by the researcher and encouraged to attend. There was a two week window after the scheduled appointment after which attendance and the data collected would be counted as the next scheduled appointment and the previous appointed recorded as a missing interview.

Data collection took place in privacy in the office of the palliative care department within the medical centre, which is separate to the clinic. On arrival to the department each participant would be given light refreshments before seeing the researcher. The researcher completed each questionnaire in turn according to the schedule of questionnaires for each interview in the participants pack. Questions were read aloud by the researcher for the participants to respond to, and written by the researcher in the participant pack, to minimise the effect of the varying levels of literacy in the sample. Upon completion or termination of the interview, participants were given 400 Kenyan shillings, equivalent of 5US\$ at the time of the study. This financial reimbursement was to ensure that transport costs were covered for all research appointments and that financial constraint was not a barrier to participation.

The researcher was also responsible for data entry into an Epidata file containing an anonymised record for each interview conducted. The researcher was requested to complete each record as soon as possible so that any errors or missing values could be identified and corrected.

Translation of study documents and cross-language trustworthiness

Data collection tools, consent forms and information sheets were translated by the researcher (available in Appendices 6 and 9). Some measurement tools had been translated and validated in previous studies, and these translations remained unchanged (208, 222).

There are many procedures and recommendations for the translation of study documents and the pitfalls of failing to ensure good translation have long been recognised (292, 293). A systematic review of quality of life measures produced a five-step guideline for translation and cross cultural adaptation of health related quality of life measures (293). The guidelines recommend that several translations should be made in addition to back translations, multidisciplinary committee review, piloting of the newly translated documents and finally weighting the scores to each cultural context (293). Unfortunately, a translation project of this magnitude was unfeasible and beyond the scope of this study and thesis due to time constraints. Instead, the study data collection documents were translated by a researcher who was a native speaker, familiar with the measures, familiar with local language nuances of the Coast region of Kenya, and experienced in palliative care research. This limitation will be further discussed in the discussion section 7.5.3.5.

Quantitative data collection tools

Data collection tools for the TOPCare trial include a demographic questionnaire, the APOS (208), the MOS-HIV (294), the GHQ-12 (295), CSRI (296), and some brief questions assessing risk behaviour and adherence. For the purposes of this study, the MOS-HIV, the GHQ-12 and two APOS items (ability to share feelings with friends and family and worry) will be analysed for data on mental health and well-being. The CSRI was used to monitor the content on the clinical encounters delivered by the study nurses, for comparison with standard care and to identify areas of effectiveness. Examples of all quantitative data collection tools can be found in Appendix 6.

Demographic questionnaire

The demographic questionnaire collected data on gender, age, partner status, number of children, number of financial dependents, highest educational attainment and possession of a number of items which were taken as asset based indicators of wealth. These indicators were the materials of which floors, wall and roof of their home were made, their water source, fuel source and whether participants possessed a fridge, bicycle, television, car or radio. Asset base approaches to determining wealth are commonly used in LMIC, as wealth and economic exchange may not be cash based and therefore estimates based on payment, salary or cash expenditure may be biased (297). This measure of wealth was developed for use in demographic health surveys by MEASURE DHS in collaboration with ORC Macro, for international use (297). The variables of asset ownership are

analysed using principal-components factor analysis to create a continuous score, which is then divided into quintiles to represent relative socioeconomic status for analysis. This method has been used widely in demographic health surveys as an indicator of wealth in Africa and elsewhere (298).

Medical Outcomes Study – HIV (MOS-HIV)

The MOS-HIV was developed from the initial Medical Outcomes Survey (MOS) in 1997 (294) and has been adapted from the MOS as a quality of life measure specific for HIV positive populations (299).

The MOS-HIV is a 35 item self report quality of life survey, which assesses participant reported function and well-being in eleven subscales. Item scores are then weighted to generate subscale scores measuring quality of life in terms of mental health (MHSS) and physical health summary scores (PHSS), which have also been validated in the African context (300, 301). MHSS is being used in this thesis to measure psychological quality of life. The MHSS is on a scale from 1-100 with a standardised mean of 50 for the general population. Psychometric analysis of the MHSS indicates good internal consistency (0.94), test re-test reliability (0.6), sensitivity to change ($p < 0.001$) and acceptable intra class correlation (0.53) (301). It has been validated in the United States (301, 302), several European countries (303), Zimbabwe (304), Uganda (305) and Rwanda (306). It is an appropriate choice of measure as it is disease specific and validated in populations from countries in SSA.

MOS-HIV data is reported on a ranking system, generating ordinal data. The raw scores for each sub-scale are transformed onto a scale of 0-100 according to guidance from the developers of the MOS-HIV (307). Because the data generated is ordinal, and because the data is a subjective report, conservative measures should be used in the analysis, therefore the data was treated conservatively. Assumptions were always tested for each statistical analysis and if found to be violated for parametric statistical analysis, data was analysed using nonparametric techniques.

General Health Questionnaire - GHQ 12

The GHQ-12 is a measure of psychiatric morbidity, and is a reduced form of the GHQ-60 (295). It has been validated in Nigeria, Kenya and Japan and is widely used in health research (308-310) and for screening in community healthcare settings (311-313). It consists of 12 questions concerning concentration, worry, usefulness, decision making ability, feeling under strain, feeling helpless, ability to enjoy day to day life, ability to face problems, depression, self confidence, feelings of worthlessness and happiness (295). Participants are required to rate each item on a Likert scale with the choice of: not at all, no more than usual, more than usual and much more than usual.

Following recommended practice, the chronic GHQ scoring method will be used to analyse the GHQ-12 data for this study (CGHQ). This method is designed for people living with chronic conditions, whose 'no more than usual' or baseline is likely to reflect levels of psychiatric distress higher than those expected in a well population (311, 314). Using this method, a report of 'no more than usual' is taken as indication of chronic illness rather than good health (314).

Because of the many versions of the GHQ (GHQ-60, GHQ-30, GHQ-28, GHQ-12 (315)) and the many different scoring methods (simple, Likert, CGHQ, GHQ (316)) comparison of results across studies is problematic. The threshold for case definition varies depending on cultural context and disease group, and unless proportion of "caseness" is necessary for comparison purposes or to assess the mental health of the sample, and has been independently validated in a target population, this approach has limited value (316). This study examined associations between high or low score and clinical and demographic independent variables, therefore raw score were used in the analysis of this data. This score is a summation of the responses of all 12 questions in the GHQ-12 and ranges from 0-12, with 12 being the worst possible score, indicating a status of severe psychiatric morbidity.

APOS items

The APOS is a multidimensional palliative care assessment tool, adapted from earlier versions of the Palliative Care Outcomes Scale (POS) and validated for use in Africa (49, 208, 317, 318). It is a seven-item measure covering physical, psychological, social and spiritual dimensions of care. There also are questions to ask of the carer of the participant which were not analysed in this study due to low availability of carers. Participants respond verbally, or by using their hand to indicate the severity of each problem, with each finger counting as a point on the Likert scale, and a closed fist as 0. Scoring is on a Likert scale of 0-5, from no problem to overwhelming problem for each item. Four items use 0 as the worst case scenario, where there are no problems. Three items are scored in the reverse, where 0 represents best case scenario or no problems. This ensures that care and attention is given to all questions.

The APOS has good face validity and is responsive to change, has moderate internal consistency as expected in a multidimensional measure and takes 5-7 minutes to complete (208).

Two items within APOS were used to address the objectives of this study: feeling worried and the ability to share feelings with friends or family.

Client Services Receipt Inventory – (CSRI)

The version of the CSRI used in this study is a modified version of a tool developed in mental health research, to assess cost and utilisation of mental health services (296). The tool was modified to

create dichotomous outcomes reporting receipt or not of components of healthcare in four domains: spiritual, psychological, nursing/medical and social.

4.4.2. Phase 2: Semi structured interviews

4.4.2.1. Participants and sampling

Preliminary analysis of the quantitative data showed that participants in both intervention and control groups reported benefit over the study period; therefore the sampling pool for phase 2 of the study included the full TOPCare sample of participants to understand the experience of participation in each study arm. The sample was purposively chosen based primarily by allocation to study arm and secondly by participant experience in terms of response to participation in the study.

The tension in sample size decisions in qualitative data collection and analysis lies between the need to be large enough to capture diversity of experience within the full sample, and small enough for detailed analysis to be feasible (285). A sample size of 30 was chosen for this study, with the expectation that this would be sufficient to achieve data saturation without creating an unwieldy dataset (285). In selecting the sample, participants who received the intervention were purposively oversampled (20 intervention participants) to explore variation in the active ingredients of the intervention. Ten participants who received the standard care were also included to further explore the therapeutic aspects of participation, beyond receipt of the intervention.

The participants were purposively sampled based on their quantitative response to participation in the study in terms of clinically significant change measured by the MOS-HIV MHSS, defined as a change in 10 points (307). A binary variable was created, identifying those who improved by 10 points or more and those did not. In terms of clinically significant response to the study, the sample for phase 2 purposively included 10 of participants who did not report clinically significant improvement (n=6 from intervention group) in addition to 20 who did (n=14 from intervention group), to explore their experiences and any potential facilitators or barriers to benefit. Further to this, deviant cases, reporting clinically significant deterioration during the study period, were purposively selected for inclusion. This technique helps to create a fuller understanding of the process of change observed (319).

Participants were selected a minimum of one month after exit so that they had received at least one appointment in the standard care clinic before the interview, and therefore all could compare their experiences in the study with standard care. The time period also provided some time for the participants to reflect on their participation in the study and how it may have affected them.

Participants were not recruited beyond 9 months after study exit to minimise recall bias. Potential participants were contacted by the researcher to enquire whether they would be interested and available to discuss their experience in the trial. The recruitment consent and data collection of this phase was completed by October 2012 (patient information sheet and consent forms in Appendix 9).

4.4.2.2. Data collection

Selected participants were contacted by telephone and if they consented at this stage, a time and date was chosen for the interview at a convenient time. On attending the palliative care department for the interview, they were given another information sheet detailing the purpose of this phase of data collection and details of data protection and their right to anonymity. If they were still happy to proceed at this point, they were given another consent form to sign and the interview was conducted in a private place.

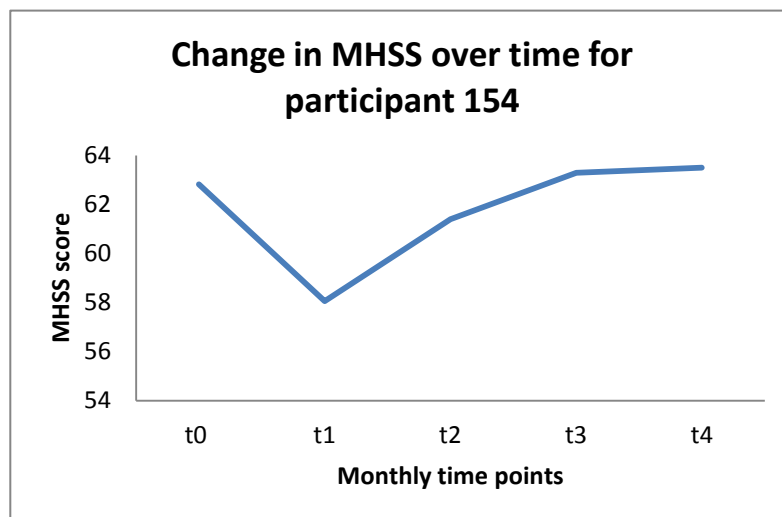
Interviews were digitally recorded and lasted 20 to 60 minutes. Participants received light refreshments and transport money as previously, for hospitality and to remove financial barriers to participation.

Qualitative interview topic guide

A topic guide was developed in collaboration with local and international researchers experienced in this area of study (Appendix 10). It was piloted for flow and comprehensiveness with one participant prior to data collection. It was amended slightly following the piloting exercise to re-order the topics for improved flow. It was structured chronologically to assess the participant's perspective of their situation before, during and after their participation in the study, with different variations for control and intervention participants to reflect their different exposure.

Initial questions asked participants about the quantitative data outcomes they had reported. A graph presenting their psychological quality of life (as measured by the MOS-HIV MHSS) over the study period was created for each participant (example in Figure 14). The researcher presented the graph and explained the data in an appropriate way, according to their level of educational attainment, ensuring understanding. The participant was then asked if this appeared to be a true story of their journey or trajectory during the study period, and to describe what was happening in their life, which may have prompted the changes seen. For example, if presented with Figure 14, the participant would be asked if they could remember something happening during the study period to explain the dip in psychological quality of life at time point 1.

Figure 14 Sample trajectory of an intervention participant as measured by MHSS, used in qualitative data collection



All participants were asked why they thought their well being had improved or deteriorated, and to what they attributed any change (objective 4). This was particularly relevant when interviewing the 'deviant cases', whether they received the intervention or not.

The topic guide then covered the participants' physical, emotional, social and spiritual wellbeing before the study began. They were asked to describe the effect their wellbeing had on their ability to perform the activities of daily living, such as work or other responsibilities. The participants were then asked to describe their wellbeing during the study and after the study had ended, using the same pattern of questions (objective 3).

After this account of experiences before during and after the study period, both study arms were asked about the experience of taking part in a research study. They were asked how easy it was, how it made them feel, and how the experience of participating in the trial might have affected them emotionally, spiritually or physically (objective 4). They were then asked about what they thought was the most important aspect of the intervention or of their participation in the study, what they attribute any benefit to and any additional comments they might have.

Participants allocated to receive the intervention care package were asked additional questions about the experience of receiving the intervention. This included components they found helpful or important to their well-being, which components they attributed improvement or deterioration to and the key differences they identified between the intervention care package and standard clinic care (objective 4). A full copy of both topic guides is available in Appendix 10.

Topic guide translation and cross-language trustworthiness

The interview topic guide was translated into Kiswahili by the researcher in Kenya, who is a native Kiswahili speaker, but from Nairobi, where a slightly different Kiswahili is spoken in Mombasa. The translation was checked by a Kiswahili speaker in the UK, who was from the same region in Kenya as the participants, and therefore was familiar with the linguistic forms and expressions of this area. Comments from the Kiswahili speaker in the UK were passed to the researcher, who refined the topic guide in light of potential misunderstandings highlighted. This was done to increase the validity of the topic guide, in recognition of the potential loss of data quality when translation is inaccurate (272).

As I do not speak Kiswahili, transcripts were translated into English prior to analysis. Steps were taken to minimise any bias or loss of meaning as a consequence of translation (269). Transcription and translation was performed by professional translators using the elance.com website. Once the job was posted on the website, four translators offered their services. All signed a confidentiality agreement before translating any audio files, to protect the identity of the participants' involved (blank copy available in Appendix 11). Once this agreement was signed, translators all transcribed and translated one file, the quality of which was checked and assessed by the researcher who conducted the interviews. The two translators who provided the transcript of the highest quality, in terms of accuracy were chosen to translate the remaining files, first transcribing the interview verbatim (in Kiswahili) and then translating the document into English.

The translators were given guidelines to follow when transcribing the documents. These included transcribing verbatim, including pauses and non verbal communication such as laughing, highlighting sections which were unclear in the recording and requesting clarification and anonymising the data.

The number of translators was minimised for more consistent translation and to increase internal validity of the translations (268). Both chosen translators were native speakers and experienced in the translation of medical research and documentation from Kiswahili into English. On completion, all transcripts and translations were checked by the researcher who conducted the interviews against the original audio recording, for accuracy and fidelity. She made only a few simple clarifications and corrections, as the transcriptions and translations were deemed to be of a high quality.

4.4.3. Data quality

During the course of the study, Skype calls were held between the study site and the PI (Dr Richard Harding) and other senior investigators at KCL and in Nairobi, a minimum of once a month. During

these calls the study team (researcher, two study nurses) would update the coordination team regarding numbers screened, recruited and exited for that month and discuss any matters arising (checklist for meetings in Appendix 2).

In addition to this, throughout the study I was in almost daily contact with the researcher and research nurses, by email and phone. The researcher entered recruitment data for each day's screening activities into an Excel spreadsheet and sent to me weekly for checking. The spreadsheet included the daily and weekly totals of numbers of participants screened, eligible, consented, randomised to each study arm and exited. The file also contained a graphic which communicated study progress in terms of recruitment and participant exits to the study team. Each week I would examine recruitment progress and the content of the database for consistency, coherence, values out of the specified or expected range and missing values. I would request clarification and double checking of the original records if this arose. In this way the data was maintained at the highest quality and the amount of avoidable missing data was reduced. A screen shot of this excel file is available in Appendix 12.

In July 2011, after the recruitment of 38 participants to the study, it became apparent that the recruitment and screening procedures were not being followed as detailed in the protocol. Recruitment was stopped while I travelled to the study site and conducted a rapid assessment of the situation. I found that screening according to the protocol was difficult due to the pressures and structure of the clinic and its context. For example, that there were seven clinic triage nurses, concurrently triaging patients.

In close collaboration with the clinic management and staff and the study team we devised a way to recruit and consent participants within this context, respecting both the study protocol and the constraints of the clinic. The intervention participants recruited to this point continued to receive the intervention as promised, but their research data was not retained. Recruitment was restarted once these procedures had been clarified, confirmed and agreed with the clinic management and study coordinators.

4.5. Ethical issues and approvals

The TOPCare study was approved by the KCL ethics committee (Reference BDM /10/11-3) and the ethics board of KEMRI (Kenyan Medical Research Institute) (Reference KEMRI/RES/7/3/1) both can be found in Appendix 4.

Additional ethical approval was sought and gained from KEMRI and KCL for the qualitative data collection interviews and analysis conducted for this thesis, again to be found in Appendix 4.

There was a distress protocol which was employed if a participant became distressed during the data collection. The participant would be asked if they wanted to pause or stop the interview, and given time to regain composure before continuing if they so wished. The participants were aware that they could terminate the interview at any time, and experience no consequences in terms of care or treatment. Participants were made aware that if the researcher became concerned about their welfare (i.e. suicidal thoughts or abuse disclosed), she would first seek their permission and then refer to the study nurses or other appropriate external support.

4.5.1. Ethical data management

The consent forms and a list of participant ID numbers and names were stored separately to the study data to ensure anonymity. The participant packs, recording the quantitative data, were stored in a locked filing cabinet during the data collection phase and were stored in the offices of the national palliative care association after data collection and data entry was complete.

The audio file for each participant was sent to me at KCL and stored on my password protected computer, and backed up on the department server for security.

4.6. Analysis

The analysis plan explains how the datasets generated in phase 1 and phase 2 are presented and described and the analysis which was conducted to address each study objective.

4.6.1. Phase 1: Longitudinal quantitative data

The following sections contain an analysis plan for the description of the database generated in phase 1 of the study. This includes analysis of recruitment, missing data, variable type and the characteristics of the sample and descriptive statistics for the demographic and clinical variables collected at baseline and baseline data for the APOS to describe their clinical status in more detail. Stata v10 was used for all analysis. The data flow was reported in accordance with the CONSORT guidance (289).

4.6.1.1. Missing data

Missing data was assessed as missing at random (MAR), missing completely at random (MCAR) or missing not at random (MNAR) in line with best practice (320). The best case scenario is that data is MAR, or MCAR, which will have no bearing on the final outcome and therefore can be disregarded (321). When data is MNAR this suggests a systematic missingness which may introduce bias, and

cannot be ignored in the analysis (321). The effect of missing data on outcomes increases with extent of missingness and the extent to which it is MNAR (320).

The missing data analysis in this thesis examined the number of items missing (single questions), number of units missing (missing all questionnaires for that time point), and the number of participants who exited the study prematurely, and reasons suggested for this if available. This contributes to an assessment of implication severity of the missingness (320). Because the sample became very well known to the researcher it was anticipated that reasons for missingness would be available and collected whenever possible in order to understand the extent of the problem of missing data in this dataset. Missing data was summarised by study arm and number of data points missing as in Table 4-4.

Table 4-4 Partial template for the summary of missing data

Status at each month	Missing data type	Control	Intervention	Total control and intervention
Baseline	Missed single questions			
	Missed single questionnaire			
	Missed interview			
	Premature exit			
	Deceased			
Month 1	Missed single questions			
	Missed single questionnaire			
	Missed interview			
	Premature exit			
	Deceased			

Management of missing data

Because of the close monitoring of this data set as it was collected, large amounts of missing data were not anticipated. The European Medicines Agency have issued guidelines on the management of missing data in clinical trials, and recommend if single items are missing within the dataset, they are imputed using the horizontal mean method, and if final data points were missing, they are imputed using last value carried forward (322). This is in line with recommendations from the palliative care literature (305).

An acceptable level of missing data is difficult to define in statistical terms as much depends on the nature of the data, the type of missingness and of the research subjects. Thompson and Levy suggest that aiming for less than 2% missing data means that the findings will be less susceptible to rejection on the grounds of bias from missing data (323). However, they also recognise that this is a very high standard and is potentially an unrealistic expectation of many clinical trial datasets.

If more than two data points were missing for any one participant, or more than 5% of the data, list-wise deletion was considered, i.e. removing all the data from all time points for the participants who exited prematurely or died. List wise deletion, while simple and transparent, is problematic for two reasons: loss of statistical power and introduction of systematic bias (321, 324). To assess the extent of bias introduced, if more than 5% of missing data was identified, list-wise deletion would be performed and the analysis repeated with this reduced dataset. If the two analyses resulted in different outcomes, this suggests that the data was not MCAR and removing partial data would cause systematic bias. In this case the partial dataset, before list-wise deletion, would be preferential, and should be used and these findings reported in the results. If there were no differences in the findings, indicating no bias introduced as a result of list wise deletion, the database participants without complete data were removed and not included in analysis.

If more than 10% of data was missing in this study, list-wise deletion would irretrievably compromise the statistical power of the study and intent treat analysis, therefore multiple imputation techniques would be explored (325).

4.6.1.2. **Variable type**

Decisions were necessary regarding the nature of some of the variables, to choose the most appropriate and valid analysis technique.

Dependent variables

As described in section 4.4.1.2 this dataset contains data on four dependent variables: psychological quality of life (from MOS-HIV MHSS), psychiatric morbidity (from GHQ-12) and worry and the ability to share feelings with friends and family (from APOS).

Because all outcome measurement tools use a Likert scale to measure the subjective experience of living with HIV, the data is described as ordinal. This means that the data is not expected to conform to the numerical normal distribution, and so it is expected that assumptions of parametric analysis techniques will be violated and analysis will be conducted using non-parametric techniques for ordinal or categorical data. This will be tested when appropriate and results reported for transparency.

Independent variables

Interval independent variables

This dataset contains six independent numerical variables: age in years, number of children, number of financial dependents, CD4 cell count, number of days since HIV diagnosis and number of days on ART.

Ordinal independent variables

There are two ordinal variables in this dataset: highest educational level attained and wealth.

Participants were asked to report whether they had never attended school, attended four years or less, completed primary school, completed secondary school or completed a diploma or higher level of education.

Wealth is a numerical variable, containing data from the demographic questions, including the material your house is made from, the type of water source available to the household and about possession of certain items which indicate a higher socioeconomic status, in this case a fridge, a bicycle, a television a car and a radio. These items were selected by the researcher, in collaboration with the study nurses as an indication of relative wealth in this population. This data is weighted and transformed using an equation used in demographic health surveys, to generate a wealth variable, which will be divided into 5 quantiles and analysed as an ordinal data (297, 298).

Binary independent variables

There are four nominal binary variables in this data set - partner status, gender and receipt of TB treatment. Partner status refers to whether they currently cohabit with a partner, whether married or not. Receipt of TB treatment refers to whether they are currently receiving TB treatment, not whether they have ever received it. In the data collection the question "Have you ever received an AIDS diagnosis?" was asked, but as all but one respondent had received this diagnosis (1/120), this question was omitted from the analysis.

4.6.1.3. Intention to treat analysis

The data was analysed using an intention to treat approach. Regardless of protocol compliance or completion, with an intention to treat approach all available data are analysed for all participants according to the study arm allocation (326). This is to ensure that available data from participants who withdrew from the trial prematurely are included in analysis, to reduce the possibility of bias in the treatment effect which could otherwise be distorted and appear more favourable than reality (327).

4.6.1.4. Sample size

The primary outcome of this thesis is a statistically and clinically significant difference in the MOS-HIV data: a measure commonly used, adapted to a HIV positive population, and validated in the cultural context. It is essential to ensure that the TOPCare study sample had adequate statistical power to detect the clinically significant 10 point change (307). I re-performed the calculations to assess the statistical adequacy of power with this sample size.

Power to detect change in outcome scores depends on the magnitude of expected change, which is usually taken from previous research in similar groups (328). There are no pre-existing thresholds for clinically significant change in the literature on which to base the sample size calculations for the GHQ, particularly when using the chronic GHQ scoring method, or the APOS item. For this reason, despite their importance as secondary outcomes, no sample size calculations were performed for these outcome measures. This avoided the risk of discarding data as statistically insignificant and therefore inconclusive, based on an untested and possibly arbitrary level of statistical significance (329), particularly when it might be more clinically useful to understand degrees of likelihood of a true causal effect (330). Findings were instead discussed with careful interpretation of magnitude and direction of effect size, and knowledge of the clinical context to counter the risks of misinterpretation.

The TOPCare study sample size was originally calculated using the APCA POS pain item as a primary outcome and the MOS-HIV as a secondary outcome for psychological well-being (290). This was performed based on data from a study in a similar patient population also in Kenya, which cited a six point change in MHSS score as clinically significant (331). This calculation identified the sample size required to detect a six point change as 56 patients per study arm with 80% power using the prescribed standard deviation of 10. Subscale scores for mental health generated by the MOS-HIV are transformed onto a scale of 100, with 50 as the mean and a standard deviation of 10 points (307). According to the developers of the MOS-HIV, a change of 10 points on a scale is “almost always likely to be meaningful”, interpreted here as clinically significant (307).

Baseline data from the TOPCare trial report a mean score of 43 on the MHSS and a standard deviation of 10 for the whole sample. Therefore, an anticipated final score of 53 (baseline plus clinically significant change) for the intervention, and 43 for the control, was used in these calculations. It was anticipated that the sample will experience some regression to the mean, as they were recruited on the basis of moderate to overwhelming pain or symptoms, but as the sample

was randomly allocated to study arms, this should be equal in both arms and therefore can be disregarded in this calculation.

The sample size calculation in Table 4-5 assesses the required sample size to detect a difference in means between control and intervention group, with 90% power and an acceptable alpha error of 5%.

Table 4-5 MOS-HIV MHSS sample size calculations

Control mean	Intervention mean	SD	Precision	Power	Total sample size (equally distributed by arm)
43	53	10	95%	90%	44

These calculations indicate that a minimum sample size of 44 would have 90% power to detect a statistically difference of 10 points between the control and intervention study arms.

In addition to analysing the data at monthly time points, as the data is longitudinal repeated measures on the same patients, analysis will also include longitudinal hierarchical modelling. This longitudinal analysis approach appreciates the value of repeated measures over time, and also will adjust the data for bias introduced into the results due to data correlation by patient, which would otherwise invalidate the findings (332). This technique will be discussed in further depth in section 4.6.4.2.

Sample size calculation for longitudinal analysis of repeated measures, correlated by patient is not straight forward as it depends on the size of the groups, the number of groups, and the intraclass correlation (ICC), which influences the design effect. However, the literature on hierarchical linear modelling, also suggests that regardless of the level of correlation, an acceptable standard error can be generated from a minimum of 100 groups with 5 observations per group (333). This indicates that the TOPCare study sample size, of 120 groups (participants) with 5 observations each will be sufficient.

4.6.1.5. Baseline characteristics

To increase familiarity with the dataset and examine the distribution of covariates between control and intervention study arm, the baseline characteristics were described in detail.

This description of the whole sample and of the results of the randomisation will not include hypothesis tests because, if performed effectively, any difference observed in the distribution of variables at baseline will be a random phenomenon (334). Hypothesis tests of randomisation do not

identify whether randomisation was performed correctly, but whether the difference observed occurred by chance (335-337). The important question is whether any observed difference between groups will bias the outcome (336, 338). Covariates with strong prognostic value, if imbalanced at baseline could bias findings, but it is better to identify an imbalance at the study design stage rather than during baseline analysis, and to use stratified sampling to adjust for this effect (334, 336).

If covariate imbalance was observed at baseline between control and study arm summary measures, and it was thought that these variables could have a strong prognostic effect on psychological and social outcomes, the variables were entered into multivariate models constructed during the analysis, to assess for effect. If no effect was seen they were omitted for a more parsimonious model.

4.6.2. Phase 2: Semi-structured qualitative interview data

This section will outline the overall approach to and process of analysing the qualitative interview data, and steps taken to ensure data quality. Specific analyses conducted to address each of the objectives will be described in detail in sections 4.6.5.2 and 4.6.6.

The qualitative data was analysed using thematic analysis using the software programme Nvivo10 to manage the data. Analysis was informed by a critical realist theoretical philosophy (section 3.3.2.2) which acknowledges the existence of truth and objective reality external to the individual, but also that these concepts are shaped and perceived through the lens of social context, emphasising causal mechanisms and social process (244, 339).

4.6.2.1. Presenting the sample and coding framework

First, the mean, median, longest and shortest length of interviews was reported with comparison between control and intervention arm participants. The transcription and translation process were briefly described.

The baseline characteristics (age, gender, partner status, number of children, number of financial dependants, educational attainment, CD4 at baseline, TB diagnosis, AIDS diagnosis, ownership of a bicycle, fridge, TV , car or radio or and clinical improvement during study in terms of MHSS) of the qualitative sample were summarised using descriptive statistics and presented in a table.

The finalised coding framework was described, describing the major themes which emerged from the data.

4.6.2.2. **Analysis approach**

In this study, thematic content analysis was used to systematically classify the data through coding and the identification of themes and patterns of meanings across a dataset (339, 340). It is an iterative process, which requires careful and meticulous constant comparison between the data and the emergent coding framework, and openness on the part of the researcher to revise any analytical decisions made, in light of new information from the dataset.

Following Hsieh, the specific type of thematic content analysis used in this thesis is directed content analysis, which takes the middle ground between open-ended inductive analysis, where there are no deductive codes at the outset, and more closed analysis in which all codes are predetermined, and analysis takes the summative form of counting (340). A combination of deductive and inductive coding in directed content analysis can be used to validate or elaborate and extend a pre-existing theoretical framework (340).

This use of thematic analysis in combination with the quantitative outcome data is in line with the critical realist paradigm of the thesis, which acknowledges both the empirical observable reality, but also the importance of subjective understanding and the importance of context in interpretation (262, 339). The deductive codes were based on objective content of the intervention (assessment of physical, psychological, social and spiritual symptoms), whilst the inductive codes acknowledge the co-existence of the more subjective interpretation for each individual which emerged as these accounts were explored.

The use of both deductive and inductive coding will ensure that unanticipated findings were also captured. This is particularly important as the concepts of psychological quality of life, psychiatric morbidity and social well-being are complex and multifaceted, and therefore may be interpreted and understood in different ways by participants.

4.6.2.3. **Analysis process**

A project journal, in a memo in Nvivo, (extract available in Appendix 13) was created before analysis commenced for recording analysis decisions and emergent findings particularly relating to the active ingredients and their mechanisms of action. Throughout the analysis, concepts arising from the data modelled and documented in the project journal. This enhanced the trustworthiness of the findings, and the “auditability” of the analysis process (341). The steps involved in the analysis are described below.

Familiarisation

Before beginning any coding of the data, each interview transcript was read through, to become familiar with the data, whilst noting down interesting passages and thoughts (339, 342). Patterns, concepts and meanings identified during initial reading were documented in the project journal for later exploration (339).

Attributes and analytical categories

To prepare for analysis, each interview transcript was assigned attributes depending on demographic and clinical characteristics of the participant who gave the interview, which would be used later in the analysis process. These attributes were chosen based on the characteristics associated with variation in response in the literature and quantitative findings: gender, poverty, education and age by decade. In addition participants were assigned a binary attribute based on presence or absence of evidence for clinically significant improvement in MHSS score during the study period (307). These attributes were included to potential demographic influences on response so the intervention and participation in the study could be explored.

To further prepare the data for analysis, 'study arm' and 'stage of study' were created as analytical codes. This ensured that the data could be examined by either study arm and at any stage (before, during and after the study). All of the data in each transcript was coded according to the stage of the study that the respondent was referring to in that part of the transcript and according to study arm.

Coding framework

The coding framework organises structures and collates the codes, into major themes and sub themes (342, 343). In this analysis plan, a code is a category assigned to the raw data, which captures the essence or otherwise summarises the content of the data (344). Themes were defined as codes or collations of codes containing elements which represented a patterned response or concept within the data (287, 339). The decision as to what constitutes a theme was based on significance and "keyness" in terms of addressing the objectives, and on the extent of repetition across the dataset (339, 343). Following Barbour, to identify themes, the following questions were posed, with constant reference to the study objectives: "Which codes are repeated? How do they relate to each other? Do these codes relate as sub themes or associates in that they occur simultaneously?" (343). Once identified, themes were grouped into major themes and sub-themes in a hierarchy, according to meaning and relationship to each other, to reduce the volume of data and structure it, making later analysis clearer and more transparent (339, 345).

Development of codes

Deductive codes were identified from the literature and included in the wording of questions in the topic guide for the interviews, or otherwise arose from the results of the quantitative data analysis (343). The literature used for identification of the deductive codes included the WHO definition of palliative care: physical, psychological social and spiritual well-being (59), and the systematic review I performed, which identified: sadness or depression and anxiety (15). Coding was performed line by line, with the deductive codes applied as appropriate. Additional themes not included within the deductive codes arose and were classified as new inductive codes (340). The inductive codes were developed iteratively, using the constant comparison method, assessing whether the codes created were useful or would be more useful if broken down further (343). This sometimes required broadening the scope of a code, to capture a concept more completely or encompass similar codes, or dividing and creating new codes if it was recognised that a concept was more complex, and required more detail (342). Fine-grain analysis was also performed on themes of particular interest to the study (342). For example, data coded at 'psychological symptoms' was explored in detail to identify fear, or worry or sadness for example, and then further examined to distinguish fear of death, fear of deterioration, fear of disclosure etc. (340). As many new codes were created as necessary to reflect the nuances of the data (287). Each code had a clear description attached, describing the content of the code to reduce overlap between codes and confusion in the coding process.

Finalising and applying the framework

Once no new codes were being identified or developed, the coding framework was finalised. Once finalised, it was applied to each transcript again, to ensure that all data had been consistently and correctly coded.

Interrogation of the data

Once finalised, the findings of the quantitative data were used to interrogate the qualitative data using the attributes and analytical categories.

This will be described in detail by objective in sections 4.6.5.2 and 4.6.6 .

Presenting the results

Findings were presented by objective. Quotations from the transcripts were used to demonstrate evidence for interpretations of the data, and to ensure close proximity to the data was maintained. This increased transparency of the analysis process and prevented unfounded claims (339, 342, 346). Extracts were carefully selected to communicate or elaborate an aspect of the findings: as

explanation, to deepen understanding and enhance readability (346), and to present sufficient description to allow the reader to appreciate and understand the process which led to the findings presented (347). Extracts were chosen from all interviews to ensure that all participants' views were represented.

Each extract will be reported with the corresponding participant identification number, gender, age and study arm.

4.6.2.4. **Data, analysis and inference quality**

In quantitative research, quality is marked by attention to internal validity, external validity, reliability and objectivity (348). Lincoln and Guba developed similar criteria for trustworthiness to indicate data quality in qualitative research which includes: credibility, transferability, dependability and confirmability (341, 348). Verification strategies to ensure trustworthiness in the data collection, analysis, findings and inferences, and are now discussed in turn with relation to this thesis.

Credibility

Lincoln and Guba define credibility as the naturalistic parallel to internal validity, and describe the following strategies to ensure credibility: prolonged engagement in the field, persistent observation, triangulation, peer debriefing, referential adequacy and negative or deviant case analysis (341). In this thesis, prolonged engagement in the field, and deviant case analysis were used to enhance credibility.

Prolonged engagement in the field

Prolonged engagement was conducted primarily with the study nurses and the researcher and myself, due to language and logistic constraints which prevented me from being physically engaged in the field. I maintained close contact with the researcher, closely monitoring data collection, and also whilst conducting the analysis to ensure my understanding and inferences from the data were credible. I also maintained close contact with the nurses, and benefited from their insight and extensive experience of the study population when making inferences from the data. During data collection, I conducted an intensive week-long field visit, working closely with the nurses, their palliative care mentor and the researcher to deepen understanding of the study context.

Deviant case analysis

Deviant case analysis is the active search for those who respond differently, or are outliers in terms of response. These participants were identified and examined in detail in order to add

understanding (349). This facilitated the process of developing concepts or explanations for the phenomena observed, and refined the explanations for the phenomena (341). Deviant cases identified during the quantitative data analysis will be purposively sampled, and their data examined in more detail, to find out why they responded as they did, and whether this data contributes to our understanding of the active ingredient and the mechanism of action. In particular close attention was paid to the explanations they gave for their study trajectories; their reasons for decreases, non response particularly and any relevant contextual data (350).

Transferability

Transferability is analogous to reliability, and refers to the extent to which the findings are applicable to other contexts, settings or populations. A mark of quality in terms of transferability is some level of transparency usually demonstrated by 'thick' description; Lincoln and Guba's term for a detailed descriptive account of the sample, data collection procedures and study context (341). In this thesis this descriptive account can be found in section 3.2, and within this analysis plan.

Dependability and confirmability

Dependability and confirmability are the analogues of external validity and objectivity (341). These qualities in qualitative research are often described as auditability: to what extent is the decision trail transparent, coherent and logical?

In this study, documented decisions, ideas, preliminary models and hypotheses based on the data to serve as an audit trail in the project journal (341, 342, 345, 351). This audit trail will help to identify the development of ideas and models proposing mechanism of action and active ingredient which increases transparency, allowing an auditor to trace the process of decision making and determine whether the decisions were reasonable and consistent and therefore the findings trustworthy (351). The coherency of the decisions in relation to the evidence presented indicates confirmability.

Having another researcher code the data concurrently, and checking inter-rater reliability is sometimes employed to increase the dependability of findings, however this is not an uncontroversial approach. Whilst it may expand the scope of the coding, provide some kind of reassurance through triangulation, and ensure that any confusion or misunderstanding is clarified, the added value to the project is arguable, as each coder brings their own interpretive framework (345, 352). This means that interpretation will be determined by the coders experience, theoretical background and discipline among other factors, which highlights the subjectivity acknowledged to be an integral part of qualitative research (352). This does not detract from the value of the findings from each coder, but calls into question the added value of multiple coders and inter-rater reliability,

therefore whilst the potential value of this technique is recognised, it will not be used in this thesis. I did however have input into finalising the coding framework, which was discussed along with the preliminary findings with the project team.

I will now turn to each objective in turn, detailing how the analysis of the quantitative and qualitative datasets will meet the study objectives.

4.6.3. Objective 1

To determine baseline levels of mental well-being and to examine associations between baseline mental well-being and demographic and clinical characteristics among patients with HIV on ART enrolled in a randomised controlled trial (RCT) of a nurse-led palliative care intervention.

The first step in meeting this objective was to determine the baseline levels of mental well-being. Baseline data for each outcome measure was presented in a scatter plot for MHSS and a percentage stacked bar chart for GHQ-12, APOS worry item and APOS share item, because of the difference in range of observations. This will depict data for the whole sample and by study arm. Summary statistics were also presented in a table for the entire data set and by study arm.

Analysis was then performed as in Table 4-6 to identify independent demographic or clinical variables with an association with psychological or social well-being at baseline.

Table 4-6 Analysis decisions for independent and dependent variables (326, 338).

Independent variables		Dependent variables			
Type	Variables	MHSS	GHQ	APOS worry	APOS share
Continuous/ interval	Age	Spearman correlation	Spearman correlation	Spearman correlation	Spearman correlation
	CD4 at baseline				
	Number of children				
	Number of financial dependents				
	Time since diagnosis (days)				
	Time on ART (days)				
Ordinal*	Education (5 levels)	Kruskal-Wallis	Kruskal-Wallis	Kruskal-Wallis	Kruskal-Wallis
	Wealth (5 quintiles)				
Binary	Gender	Mann Whitney	Mann Whitney	Mann Whitney	Mann Whitney
	Partner status				
	TB diagnosis				

*If any continuous variable is divided into quantiles after data type examination it will be analysed in objective one thus

If any association was identified between independent variables and any of the dependent variables at baseline ($p \leq 0.25$), they were entered into a multivariate analysis to assess for any association, using ordered logistic regression for ordinal outcomes and multiple linear regression for interval outcomes (326, 338). The assumptions of these tests were checked by assessing the normalcy of the distribution of residuals for linear regression (using Shapiro-Wilk test) and the proportional odds assumption for ordered logistic regression, which assumes that the coefficients which describe the relationship between the lowest and the higher categories have the same relationship between each group. The findings of these tests were reported to ensure transparency.

4.6.4. Objective 2

To identify any effect of the palliative care intervention on mental well-being, comparing participants receiving the intervention and standard best practice.

4.6.4.1. **Visual analysis over time and analysis at monthly time points**

The analysis was performed using the MHSS score from the MOS-HIV (psychological quality of life), GHQ-12 (psychiatric morbidity) and the APOS items (worry and ability to share feelings with friends and family). For each dependent variable, the data was first presented in either a stacked bar chart or a line graph, depending on which would most clearly display the range of values and change in status over time in each study arm. The MHSS score was presented using a line graph with the inter-quartile range, and GHQ-12, APOS worry and APOS share were presented using percentage stacked bar charts, to enable visual analysis of the distribution and change in the distribution of the data over time.

To examine response over time, intervention and control arms were compared at monthly time points to describe population level change in each study arm and to compare and identify whether one study arm improved quicker than the other (353). This analysis was performed adjusting for baseline score. Results were presented in a table with the coefficient for the difference between intervention and control study arms, 95% confidence interval for this coefficient and p value. Interval variables were analysed using linear regression, and ordinal variables were analysed using ordered logistic regression. Assumptions were checked for all analyses. If residuals for linear regression were not normally distributed, the variable was divided into quantiles and analysed using ordered logistic regression. If the proportional odds assumption was violated in the ordered logistic regression, multinomial logistic regression was explored, which is a more flexible but less parsimonious approach.

4.6.4.2. **Analysis of repeated measures**

The data is longitudinal, collected over five months. Because the observations are repeated measures, with five observations per participant, we know that the observations are not independent. This means that the data is probably correlated or clustered by participant and if not taken into account during analysis, it is possible that any observable effect would appear stronger than it truly is. To adjust for the effect of correlation, a hierarchical regression model was used. As the dependant variables are ordinal, generalised estimating equations (GEE) is the best option to produce a population level average estimation of effect of study arm (354).

To perform GEE it is necessary to first specify the correlation matrix and the link function of the data. The correlation matrix of this dataset was exchangeable, because we can assume that any two

observations from any one participant will have the same correlation (326). The Gaussian link function for linear models was used to fit the data (355).

If the residuals of this multilevel model were not normally distributed, hierarchical linear mixed level modelling was conducted using the Stata command GLLMM (Generalized Linear Latent and Mixed Models). This is a relatively novel analysis to analyse categorical or ordinal variables, accounting for correlated or clustered data over time (332, 356).

To perform this analysis the distribution used, the link function, the number of integration points for each summation and whether adaptive or ordinary quadrature must first be specified (357). For ordinal responses the link function is ordered logistic or 'ologit', with a binomial distribution (355). Adaptive integration is expected to perform better than Gaussian integration, particularly when intra class correlation (ICC) is high and cluster size is small, and with non-normal distributions as in this study (358). Adaptive quadrature captures change in a slope when it changes rapidly, in a more reliable way than ordinary Gaussian quadrature (358). The degree of accuracy is controlled by the number of integration points. Increasing integration points increases accuracy but also computational burden, and increases the risk that the software will not achieve convergence, and therefore an accurate result (357, 358). The recommended and default number of integration points is 8, which was used in this analysis (358). The GLLMM command operates more successfully if there are fewer categories of the dependent variable; therefore the outcomes were divided into four quantiles. This would also enable comparison of the effect of the intervention on all dependent variables.

The decision to analyse the data using multilevel modelling was verified by the ICC, which was calculated from the variance of the random intercept of each hierarchical model created and was reported alongside.

This analysis was performed adjusting for baseline score. Results were presented in a table with the coefficient for the difference between intervention and control study arms, 95% confidence interval for this coefficient, a p value and the ICC.

Accepting or rejecting the null hypothesis

H_0 : There will be no difference in psychological quality of life, measured by the MOS-HIV MHSS, in longitudinal analysis of difference between participants allocated to receive the intervention (nurse led HIV palliative care) and participants allocated to receive the control (standard HIV clinic care).

Analysis using GEE or GLMM is the most appropriate and sophisticated analysis and therefore was used to accept or reject the null hypothesis using the MOS-HIV MHSS data, at $p \leq 0.05$.

4.6.5. Objective 3

To determine and describe participant experience and longitudinal response to participation in the study in terms of mental health and well-being, and to identify and explore associations between participant response and demographic and clinical characteristics

Mixed methods are required to meet this objective. The analysis plan for the quantitative data will first be presented and then the analysis plan for the qualitative data, including the research questions stated in section 3.3.3.3. A plan for the integration and presentation of the data in the results section will then be described.

4.6.5.1. Phase 1: Quantitative data analysis plan

To determine longitudinal response to the participation in the study, area under the curve was calculated for each participant. This was then analysed for association with demographic and clinical variables.

Area under the curve analysis

Traditionally used in pharmacology research to assess uptake of drugs or bioavailability, the use of area under the curve (AUC) to assess treatment response in clinical trials is an increasingly popular approach (338, 359). This is due to the ability of this technique to assess the improvement of each participant taking into account the longitudinal aspect of the data and any cumulative treatment effects, creating a mean score for the study period (360).

Before calculating the AUC it is essential to assess the differences between each time-point in the data. If the time-points were equally spaced, with a standard deviation of less than half of the mean number of days between time-point, the more simple trapezoid method could be used. If the time points were unevenly spaced, a more complicated method called the integration of regression would be used (360).

The data was examined to calculate the mean time between appointments for all participants recruited to the study. During data collection the researcher was instructed to make sure all data collection occurred within two weeks of the appointment date, and if this was exceeded, the data collection was to be recorded for the next time point. It is therefore hypothesised that the time-points will be evenly spaced so the trapezoid method is described here. This involves calculating the mean score for baseline + time one, time one + time two, time two + time three and time three +

time four and summing these values to represent the area under the curve and therefore a mean value over time. This was performed in Excel and then transferred into Stata for analysis

Histograms displaying the distribution of area under the curve for all participants were reported for MHSS, GHQ-12 score and APOS worry and APOS share items.

Analysis of association

Multivariate regression analysis was performed to identify association between AUC for each dependent variable and the clinical and demographic independent variables, using linear regression for interval variables and ordered logistic regression for ordinal variables.

To check analysis assumptions for linear regression, the residuals for each regression were tested using the Shapiro Wilk test for normality. The assumptions for ordered logistic regression were checked using the proportional odds assumption. If found that the assumptions were not met, multinomial logistic regression was performed.

Multivariate models were constructed using the vselect command in Stata which lists the possible combinations of multivariate models with the corresponding r^2 , Akaike's information criteria (AIC) and Bayesian information criterion (BIC), an indication of the fit of the model and its parsimony (361). A model with a relatively lower AIC and BIC and a higher r^2 , is a model which explains the variation in the data well, with less potential for error.

Multivariate analysis was guided by the rule of no less than 20 subjects per variable in the model(326). In the event of multiple tests of statistical significance, the Bonferroni method will be used to reduce the chance of alpha error (362). This is a relatively conservative method of reducing the false positives in multiple statistical testing. It has been criticised for increasing the rate of false negatives and reducing statistical power to unacceptable levels, and so clinical judgement will also be used to assess the appropriateness of applying this correction, if it is suspected that a type II error has occurred (363). All analysis was adjusted by baseline score

Presenting the results

The final model for each dependent variable was presented in a table, presenting coefficients or odds ratios, 95% confidence intervals and p values for statistical evidence of effect. A summary of the strength and directions of all associations identified was presented.

4.6.5.2. Phase 2: Qualitative data analysis plan

Analysis of the qualitative data to address objective 3 is structured around the findings from the quantitative longitudinal analysis and the following research questions:

How do participants respond to participation in the study and receipt of the intervention, and is this response different in participants with different demographic or clinical characteristics?

Cultural understanding of the concept of well-being

In acknowledging my cultural distance from this sample, I felt it was important before beginning the analysis to first understand what the participants of this study understood by the culturally and contextually dependent concept of well-being. I recognise that this population have a very different experience of life, and of health and well-being to me, and therefore it was important to explore their understanding of the important aspects of well-being.

I performed a text search within Nvivo 10, using the search terms 'normal' well' or 'better', to identify all instances in the interview manuscripts where participants described what it meant to them to be normal, well or better and collated those extracts in a model. I attempted to preserve the participants' words, (once translated) as much as possible to retain fidelity to their descriptions and understanding of the concept. This model will be presented before the results of the analysis for objective 3, to contextualise the findings, and enhance understanding of the cultural nuances of participants understanding of well-being.

Analysis process

A descriptive analysis of how participants responded longitudinally was conducted in terms of mental health and well-being before, during and after the study.

Then the data were analysed according to participant response to the study (MHSS). This was defined using suggested 10 point change in MHSS score as an indication of clinically significant change (307). Participants who report an improvement of 10 points or more from baseline to final time-point were categorised into a binary variable of improvement. Those who improved were compared with those who did not improve. The group of participants categorised as not improving included those who did not improve or deteriorate to a clinically significant extent, as well as those who clinically deteriorated.

The qualitative results were presented in a narrative form by presence or absence of clinically significant benefit, study arm and by stage of study (before, during and after), with text extracts to substantiate any claims.

The data were also analysed according to the clinical and demographic characteristics which were found to be significantly associated with longitudinal change in the quantitative AUC analysis. The data were interrogated across these variables to highlight any exceptions and contradictions or nonconforming cases (patterns within the data) (343). Due to small numbers in some of the characteristics (i.e. only 5 men) it was not always possible to look for patterns among those who reported clinically significant benefit or not. It was anticipated that any patterns identified would elaborate or expand the quantitative findings, either through conflict or consensus.

Some variables, for example education, had several categories, and therefore to facilitate the explanation of patterns within the data, the sample was divided into two groups: those with primary school education or less and those with secondary school or higher. Wealth quintiles were combined to form a binary variable of relatively high or low wealth.

The distribution across clinical and demographic variables were also presented first in a table and then in narrative form, with text extracts to substantiate any claims.

The model of cultural understanding of the concept of well-being constructed using the descriptive phrases of 'normal', 'well' or 'better' was modified during the analysis as it became clear that associations between these descriptive phrases highlighted the barriers and facilitators therapeutic change and clinically significant benefit. This modified model was presented to facilitate understanding of the findings from the qualitative data analysis to address objective 3.

4.6.5.3. Integrating and presenting the findings

The findings from the quantitative and qualitative analysis for objective 3 were then presented and discussed, highlighting the qualitative explanation for findings from the quantitative analysis, and any incongruence or convergence in findings.

4.6.6. Objective 4

To identify and explore the existence of “active ingredients” and mechanisms of action of the intervention and therapeutic aspects and processes of study participation.

Mixed methods were used to meet objective 4 integrating findings from analysis of the quantitative data from phase 1 and qualitative data from phase 2 of the study.

First, the components delivered as part of the intervention care package and how they differed from standard care was described. Receipt of components of care was analysed for association with measures of mental health and well-being to identify the effective components. Qualitative data from phase 2 was analysed using directed thematic analysis to identify active ingredients of the intervention and their mechanism of action and therapeutic aspects and processes attributed to study participation.

4.6.6.1. **Components of palliative care delivered as part of the intervention**

The CSRI measures services received by participants throughout the study, permitting comparison of service receipt by study arm. Results were presented in a bar chart for visual comparison and then analysed as a binary variable indicating whether a participant ever received the service or not at any time point during the study period. χ^2 tests were used to identify differences in service receipt between control and intervention groups. Fishers exact test were used when there were less than 5 observations in each cell (328). A Bonferroni correction for 22 test to be performed during this analysis indicated that a threshold for significance of 0.002 would be a conservative indication of a statistically significant association (362). However, because of the concerns that use of Bonferroni corrections leads to increased type II errors, a less conservative threshold of $p \leq 0.01$ will be used as a threshold for statistical significance (363). The findings of this analysis were presented in a table reporting the test statistic and a p value.

4.6.6.2. **Active ingredients**

Phase 1 quantitative data analysis to identify the active ingredients of the intervention

The analysis of longitudinal data to meet objective 3 included the calculation of AUC for each participant, for each of the following variables: psychological quality of life, psychiatric morbidity, worry and the ability to share feelings over the study period. As the MHSS, GHQ-12 and APOS are non-parametric variables, and preliminary analysis indicated that assumptions ordered logistic regression were violated, binary logistic regression was used. A binary variable for each AUC outcome variable was created, dividing the data at the median, into two quantiles. This was used to indicate high or low AUC for each outcome variable and analysed for association with receipt of each component of care, adjusting by baseline score. Logistic regression analysis then identified components of care associated with improvements in mental health and wellbeing, as measured by AUC for MHSS, GHQ-12, APOS worry and APOS share items.

The results will be presented in a table for each outcome, reporting the odds ratio, 95% confidence intervals and p value. An adjusted value of $p \leq 0.01$ will be used as a threshold for statistical significance because of the increased risk of type II error due to multiple tests of significance (363).

Phase 2 qualitative data analysis identifying the active ingredients of the intervention

The terms 'active ingredients' and 'mechanism of action' are used when describing the intervention, as defined in section 3.3.1, in line with MRC guidelines (247). Participants were asked directly in the interviews, what they attributed any change in their well-being to, and how this attributed aspect might have an effect. This data was used as a starting point to identify any possible active ingredients of the intervention, with the rest of the interview data also examined. It is recognised that whilst participants can produce leads for the researcher to pursue, through choice of language and overt or covert revelation of underlying assumptions, researchers have a duty to thoroughly explore any leads and critically examine participant suggested concepts or logic (343).

Each active ingredient identified was created as a major theme. These were explored, described using text extracts to substantiate findings.

Summary of active ingredients

Findings regarding the content of the intervention care package were integrated with the descriptive quantitative and qualitative data analysis regarding the active ingredients of the intervention.

4.6.6.3. Therapeutic aspects of participation

As well as the active ingredients it was hypothesised that there would be contextual factors or other aspects of participation in the study which might have therapeutic benefit, beyond receipt of the intervention. These were explored in the qualitative data from participants in both the control and intervention group and are described using the terms "therapeutic aspects of participation".

Therapeutic aspects were created as major themes and sub themes. To present the findings, each therapeutic aspect of participation was first presented in a percentage stacked bar chart. Each bar chart represented the total number of text extracts found which contained data on a theme, presenting the percentage of each sub-theme demonstrate the different distribution of sub-themes across the study arms. It was then described in a narrative using text extracts to substantiate claims.

4.6.6.4. Mechanism of action and therapeutic processes of participation

To identify the mechanisms of action of the active ingredients, and the therapeutic processes associated with the therapeutic aspects of participation, the data was examined whilst asking the

question: “What was actually occurring here?” This question was repeatedly asked to examine why the identified ingredients and aspects were so powerful – why is communication reported to be so therapeutic? Why it is that compassionate care was cited as a source of relief? How might this aspect of ingredient exert its effect? These questions helped to extract the underlying processes of how and why these aspects of care were reportedly so therapeutic to participants, whilst retaining close proximity to the data.

The identified active ingredients and therapeutic aspects and processes of study participation were reported alongside their associated active ingredient or therapeutic aspect of participation, and then mapped onto the model of facilitator and barriers of mental health and well-being during participants experience of the study, which was created and then modified to address objective 3 (section 4.6.5.2).

5. Results 1: Description of the datasets

5.1. Phase 1: Longitudinal quantitative data

5.1.1. Recruitment and follow up

Recruitment was conducted with fidelity to the protocol (section 4.4.1.1) from the end of July 2011 to the end of February 2012. The researcher recruited a mean of 3.9 participants each week (range 1-8), approaching them in the CCC. A total of 2070 participants were screened over the recruitment period. Details of the recruitment statistics can be found in Table 5-1.

Table 5-1 Summary of recruitment statistics for the Phase 1 dataset

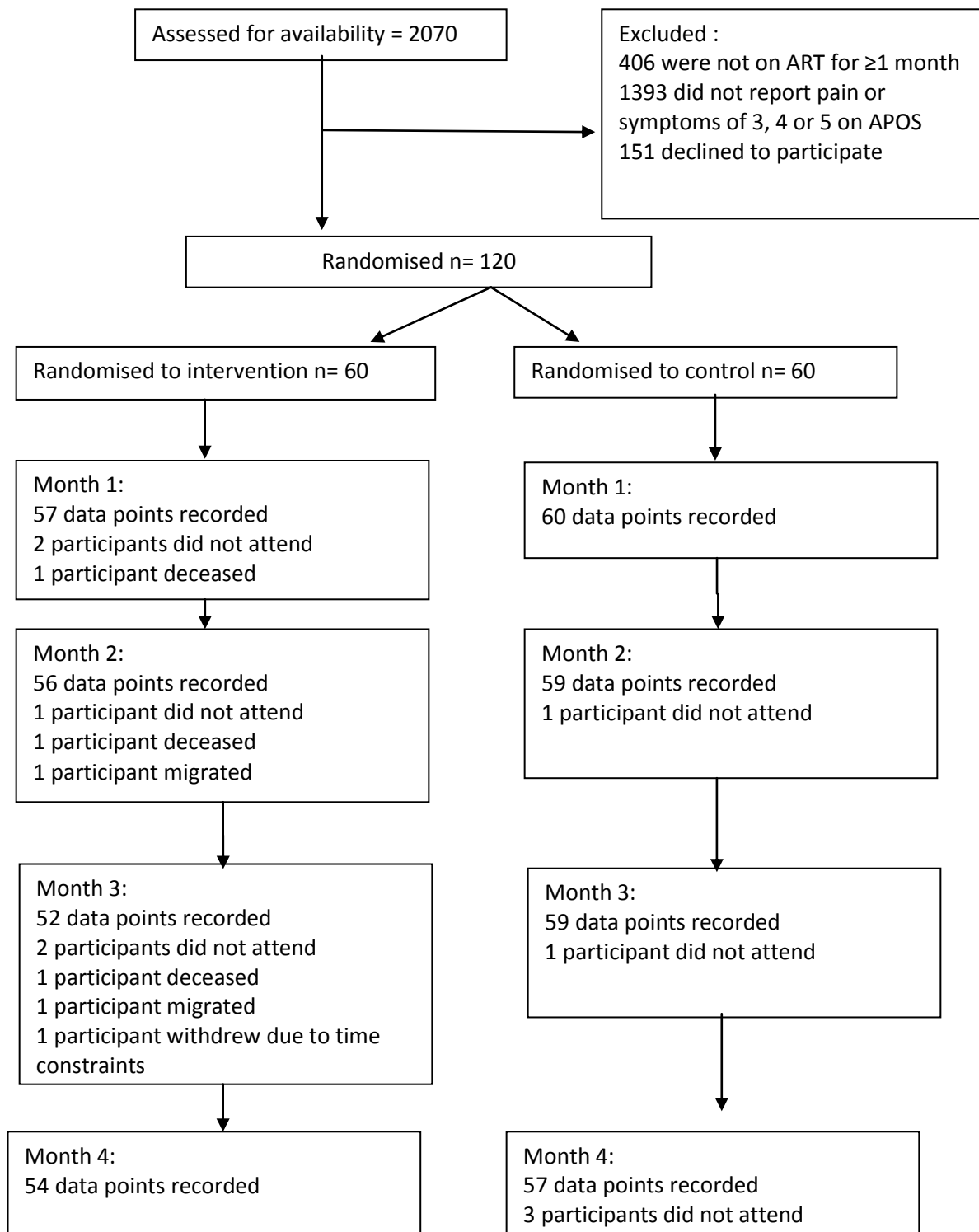
	Total screened	Total adult, HIV positive and on ART	Total participants reporting pain or symptoms ≥ 3 on APCA POS	Total invited to consent to participate	Total refused	Total consented
Actual numbers	2070	1664	271	271	151	120
Percent	100%	80% of total screened	13% of total screened	16% of total adults on ART	56% of total eligible	44% of total eligible

Thirteen percent of the total number of participants screened and 16% of all those on ART had pain or symptoms which had lasted more than two weeks and therefore were eligible for the study. The percentage of those eligible that refused to participate appears relatively high at 56%. Data on reasons for refusal was not formally collected, but informally the researcher was informed that participants often had difficulty taking time off work to attend the data collection interviews.

The follow up flow of the study participants is depicted in a CONSORT diagram below (289). Each data point represents a participant data collection appointment.

Results 1: Description of the data

Figure 15 CONSORT flow diagram



5.1.2. Missing data

Over the trial period 6 participants prematurely left the trial representing 5% of the total sample (n=120). Three participants died before the trial was complete, three withdrew prematurely (two

Results 1: Description of the data

moved away and one became less available due to work commitment). Of those participants who remained alive during the study period, 98.1% of possible data was obtained.

The sub sample of participants who left prematurely (n=6), were all allocated to the intervention study arm. They had been diagnosed more recently and had received ART for a shorter time compared with the sample median, but otherwise there appeared to be little difference between these participants and those who remained in the study. Due to the small numbers, it was not possible to perform analysis to identify whether there was any statistically significant difference between those lost to follow up and the remainder of the sample. Table 5-2 contains the clinical and demographic details of three participants who died during the study period (attrition due to death or ADD) (255).

Table 5-2 Demographic and clinical characteristics of participants who died during the study period

Reason for exit	Deceased (Cervical cancer)	Deceased (Cervical cancer)	Deceased (Malaria)
Number of data points	1	3	2
Gender	f	f	f
Partner status	no	no	yes
Age (years)	60	40	23
Highest educational level attained	Never attended	Primary	Primary
Number of financial dependents	6	2	7
Number of children	5	2	1
Time since diagnosis (years)	5	<1	<1
Time on ART (years)	5	<1	<1
Poverty quintile (1=higher, 5= lower wealth)	5	3	1
Receipt of TB treatment	no	no	no
CD4 at baseline	358	524	403
Mental health summary score (MHSS) at baseline (MOS-HIV) (1-100 range; 100 best)	12.95	36.79	56.80
Physical health summary score (PHSS) at baseline (MOS-HIV) (1-100 range; 100 best)	15.38	15.94	47.20
GHQ-12 score at baseline (Chronic scoring method, 0-12; 12 worst)	11	12	0

Results 1: Description of the data

Once it became apparent that all of the recorded deaths occurred in participants allocated to the intervention study arm, I launched an investigation with principal investigator (Dr Richard Harding). This involved close examination of the clinical records kept by the study nurses during delivery of the intervention, and interviewing the researcher and study nurses for further details to ensure that these deaths were not the result of receiving the intervention. The subsequent narratives are the result of this investigation.

The first participant who died was diagnosed with advanced cervical cancer. She was randomised to the intervention group but only received one session of palliative care before death. She would have been eligible for the hardship fund held by the hospital for those who were unable to afford chemotherapy, but her cancer was so advanced by the time it was diagnosed, it was decided by the medical team at the hospital that chemotherapy would have been ineffective. She received nutrition counselling, advice about HIV and her relatives were counselled to support her. She was admitted to the provincial hospital as she deteriorated, and was supported by the study team and the local hospice throughout, receiving opioid analgesia. In collaboration with the local hospice, the participant and her family received counselling to prepare for death and the dying process. As a result she decided that she wished to die at her parental home in a rural area. This was facilitated by hospice staff in Mombasa in liaison with a hospice team near her parental home. She died at home, with her family, as she wished.

The second participant was recruited to the trial with severe pain. She received analgesia and underwent investigations which revealed in time that she also had advanced cervical cancer. She would have been eligible for the hardship fund provided by the hospital, to pay for chemotherapy or radiotherapy, but her cancer had metastasised into other major organs and it was decided that this treatment could not be curative and would not be beneficial. She received five palliative care appointments and attended three data collection appointments before she died. As part of her palliative care she received counselling for ART adherence, psychosocial support and advice about the importance of hygiene and medication side effects. She also received opiates and other analgesia for abdominal pain and advice on diet and exercise for constipation, related to opioid use for analgesia. She was admitted twice to the inpatient ward at Bomu hospital. After her first discharge she was readmitted when she attended her palliative care appointment and it was recognised by the study nurses that she was seriously unwell. She continued to be given analgesia for pain management and was being considered for food by prescription due to her recent weight-loss when she died of complications due to her cervical cancer at Bomu hospital.

Results 1: Description of the data

The third participant who died whilst in the study was a woman who migrated after four palliative care appointments and two data collection appointments, and subsequently died in a rural area. On enrolment, she reported painful legs and some nausea, but her main concern was her husband, whom she described as abusive and drinking too much. She was otherwise well and managed a small income generation project. As part of her palliative care she received nutrition counselling and advice on family planning and adherence to ART. She had made great progress in her relationship with her husband, reporting that he had become more cooperative and supportive. She was preparing to speak with her husband, with support and guidance from the palliative care team, to attempt to convince him to attend a session of couple's counselling to encourage him to be tested for HIV. She then became un-contactable by phone, and when visited by a community health worker who had been sent to trace her, it was confirmed by community members that she and her husband had decided that she should travel north to the rural area, to work on the family farm. Her husband then reported to the palliative care team that whilst in the rural area she contracted severe malaria and died.

Whilst there is cause for concern that all of the participants who died during the study were in the intervention study arm, there does not appear to be any evidence in the narrative data from the participant records that they were put at risk by the intervention (for example lack of access to care or over medication, or domestic abuse due to participation). The other possibility is that the randomisation process was in some way compromised and that these participants were allocated to the intervention purposefully due to their visible need for palliative care. The researcher had been trained and prepared through role play for this scenario to prevent this eventuality. She was intensely supported throughout the recruitment phase of the study, with this potential temptation (to purposively allocate sicker participants to the intervention) in mind. The research team were satisfied on the basis of this investigation that the randomisation procedure was performed according to the study protocol, and was not compromised.

The remaining three participants who exited the study prematurely, (also all in the intervention arm) left the study due to migration or a lack of time to participate in the interviews, due to employment (attrition at random AaR) (255). Their demographic and clinical characteristics are summarised in Table 5-3.

Results 1: Description of the data

Table 5-3 Demographic and clinical characteristics of participants who exited the study prematurely

Reason for exit	Withdrew (migrated and then died after study period ended)	Withdrew (migrated)	Withdrew (became employed)
Number of data points	3	2	3
Gender	m	f	m
Partner status	yes	yes	yes
Age (years)	50	25	31
Highest educational level attained	Primary	Primary	Primary
Number of financial dependents	10	3	0
Number of children	4	1	1
Time since diagnosis (years)	<1	<1	<1
Time on ART (years)	<1	<1	<1
Poverty quintile (1=higher, 5= lower wealth)	1	4	4
Receipt of TB treatment	no	no	no
CD4 at baseline	473	492	322
Mental health summary score (MHSS) at baseline (MOS-HIV) (1-100 range)	20.72	48.85	44.78
Physical health summary score (PHSS) at baseline (MOS-HIV) (1-100 range)	26.49	59.60	58.92
GHQ-12 score at baseline (Chronic scoring method, 0-12; 12 worst)	8	3	8

The first participant who withdrew prematurely reported severe generalised pain on enrolment. He required a physician review and investigations. He was treated with analgesia, antibiotics, received counselling on diet and ART adherence and was diagnosed with a stomach ulcer for which he received antacids. The results of these investigations prompted further tests, by which time the participant had requested a referral to healthcare facilities in Tanzania, where healthcare is more affordable. This participant was polygamous and also had a wife and family in Tanzania. He attended six palliative care appointments and three data collection appointments before leaving. His Kenyan wife informed the study team that he had died of bone cancer diagnosed in Tanzania, after the study period had finished.

Results 1: Description of the data

The second participant attended six palliative care appointments and two data collection appointments. She reported some physical pain and other symptoms, but her main source of distress was her relationship with her husband, who was unfaithful and planning to marry a 2nd wife due to her HIV positive status. Since he was HIV negative, he did not want to take risks by being with her. She was offered advice on adherence, diet, sexual health and hygiene and given more information about HIV/AIDS. She also received treatment for thrush and TB. After her husband remarried, she decided to leave Mombasa to be taken care of by her mother.

The final participant who withdrew from the study prematurely withdrew because he became employed and was concerned that if he took time off work to attend the sessions he might not be paid or might lose his job. He was severely depressed at enrolment and socially isolated, describing himself as overwhelmed by the burdens of HIV and fears for the future. He received psychological and emotional support, adherence and nutritional counselling and couples counselling with his wife. After the first session he reported feeling much better and began to take care of himself and look for paid employment. His wife attended the clinic after he had missed three appointments, and reported that he had improved due to the support of the study nurses, had become employable as a result, and therefore had secured a job and was unable to take any time off to attend. He attended four palliative care appointments and three data collection appointments.

Again, while it might initially appear concerning that all participants who exited the study prematurely were in the intervention arm, all investigation of the clinical data and interviews with the study team do not suggest any compromise of the study protocol. I am confident that the participants who died during the study period or exited prematurely were allocated to the intervention study arm randomly, and study participation did not cause their death.

Missing items

In the total of 600 data collection appointments which could have been attended, a total of 26 were not attended, therefore for these appointments there is no data for any outcome measure (26 missing out of a possible total of 600: 4.3% missing). Whilst the figure of 4.3% missing data is low, of this 4.3%, 21 of the 26 missing data points (81%) occur in the intervention arm due to increased attrition in this group. Among the completed interviews, there was only one missing item (omitted or skipped question within the completed questionnaires). All other attended data collection appointments had complete data. The distribution of missed single interviews is evenly distributed across control and intervention study arms (five missing single interviews in each).

The distribution by study arm, and time-point is described in Table 5-4.

Results 1: Description of the data

Table 5-4 Summary of missing data for outcome measures by interview time point and study arm

Status at each month	Missing data type	Control	Intervention	Total control and intervention
Baseline	Missed question	1	0	1
	Missed single questionnaire	0	0	0
	Missed interview	0	0	0
	Premature exit	0	0	0
	Deceased	0	0	0
Month 1	Missed question	0	0	0
	Missed single questionnaire	0	0	0
	Missed interview	0	2	2
	Premature exit	0	0	0
	Deceased	0	1	1
Month 2	Missed question	0	0	0
	Missed single questionnaire	0	0	0
	Missed interview	1	1	2
	Premature exit	0	1	1
	Deceased	0	2	2
Month 3	Missed question	0	0	0
	Missed single questionnaire	0	0	0
	Missed interview	1	2	3
	Premature exit	0	3	3
	Deceased	0	3	3
Month 4	Missed question	0	0	0
	Missed single questionnaire	0	0	0
	Missed interview	3	0	3
	Premature exit	0	3	3
	Deceased	0	3	3
Totals	Missed question	1	0	1
	Missed single questionnaire	0	0	0
	Missed single interview	5	5	10
	Premature exit	0	3	3 (7 missed interviews)
	Deceased	0	3	3 (9 missed interviews)

The minimal amount of missing data is largely due to the efforts of the researcher, who worked in close collaboration with the staff and management at the study site to contact participants who had not attended their data collection appointments. Community tracers from the comprehensive care clinic, usually employed to ensure adherence to ART, were asked to enquire about participants who had not attended their appointments using their contacts and local knowledge. This collaborative approach contributed to the minimal amount of missing data and subsequent high quality dataset.

Management of missing data

When one value was missing due to a participant missing a single interview and then returning to the study, single imputation was used: last value carried forward or the horizontal mean (320, 322).

For the 6 participants who left the study prematurely and therefore had more than one missing data point for all outcome measures, list wise deletion was not performed due to the small amount of missing data. Once the single imputations had been performed, this left 16 missing data points, or 2.7% missing data. This small amount of missing data does not necessitate management (325).

5.1.3. Variable type

In terms of independent variables, age in years, number of children, number of financial dependents, CD4 count at baseline, time since HIV diagnosis in days and time on ART in days were all analysed as continuous data. Education and wealth were analysed as ordinal variables, and gender, partner status and TB status were analysed as binary variables as detailed in Table 4-6.

5.1.4. Characteristics of the sample

The demographic and clinical characteristics of the sample are reported in Table 5-5. Of the entire sample, the mean age was 39 years, and 81% were female. Most achieved primary education and had more financial dependents than children.

Results 1: Description of the data

Table 5-5 Demographic and clinical characteristics of the TOPCare sample

	Entire sample (n=120)	Control (n=60)	Intervention (n=60)
Female n (%)	97 (81)	49 (82)	48 (80)
Mean age in years (sd, range)	39 (8.9, 22-64)	40.5 (9.2, 22-64)	38.3 (8.2, 23-60)
Has a partner (% yes)	63	60	66.7
Median no. children (IQR)	2 (1-4)	2.5 (1-4)	2 (1-4)
Median no. financial dependents (IQR)	3 (2-5)	4 (3-5.5)	3 (2-5)
Education			
Never been to school	10	6	4
<4 yrs of school	3	1	2
Primary	76	35	41
Secondary	27	17	10
Diploma	4	1	3
Poverty quintile (5 quantiles of wealth), n (%)			
1 - wealthiest	26 (22.2)	14 (23.3)	12 (21.1)
2	21 (18.0)	9 (15.0)	12 (21.1)
3	23 (19.7)	9 (15.0)	14 (24.6)
4	24 (20.5)	12(20.0)	12 (21.1)
5 - poorest	23 (19.7)	16 (26.7)	7 (12.3)
Median years since HIV diagnosis (IQR)	3.5 (1.3-5.2)	4.7 (2.4-5.7)	2.6 (0.9-4.4)
Median years on ART (IQR)	2.5 (0.8-4.2)	3.0 (1.6-5.0)	1.6 (0.4-3.5)
Median CD4 count (cells/mm ³ , IQR)	358 (223-506)	343 (209-558)	359 (247-490)
Receiving TB treatment (%yes)	8	12	5
WHO stage			
Stage 1	13	4	9
Stage 2	41	22	19
Stage 3	62	32	30
Stage 4	4	2	2

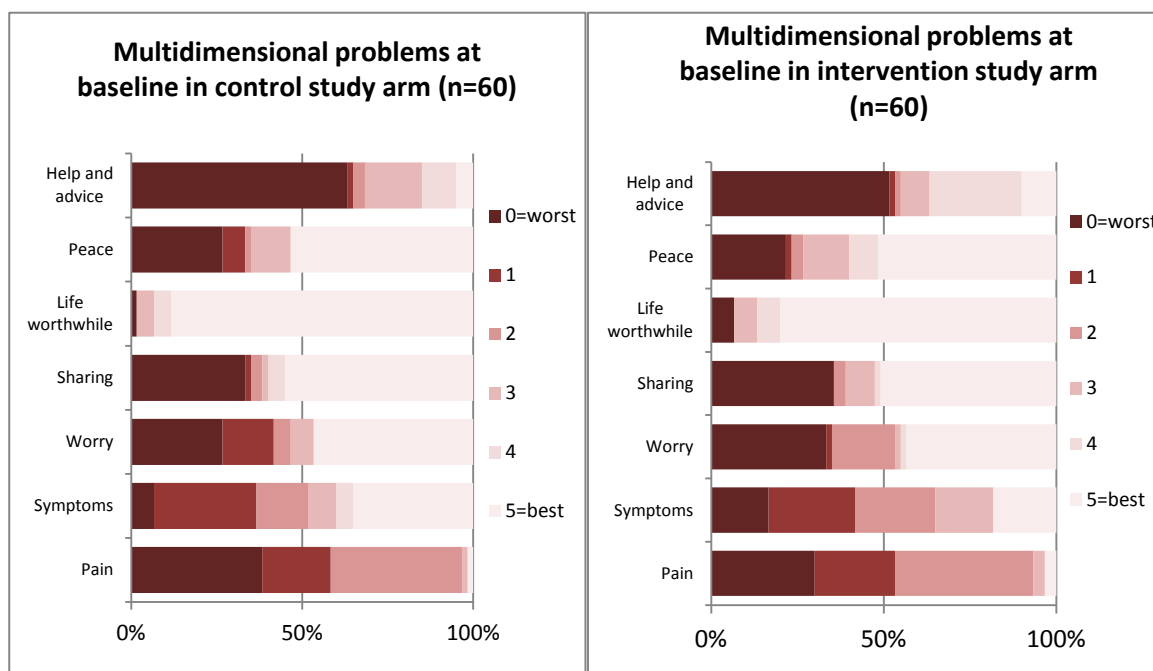
Participants allocated to the control arm were diagnosed and on ART for longer than participants allocated to the intervention arm.

Figure 16 is a stacked bar chart displaying the distribution of baseline score by percentage from the APOS for each study arm to enable comparison. In this figure, 0 indicates the worst outcome and 5

Results 1: Description of the data

indicates the best outcome (scores for items 1, 2 and 3 have been reversed for ease of interpretation).

Figure 16 Multidimensional well-being at baseline for TOPCare study participants, by study arm



Whilst pain and symptoms appear to be very problematic for the sample at this point, it is important to remember that a pain or symptom score indicating moderate to severe pain or symptoms (0-2 in this figure) were inclusion criteria for the study. Other than pain and symptoms, it appears over 50% of participants in both study arms experienced severe difficulty with getting enough help and advice to help their family and friends plan for the future and that over 20% in each arm reported that they had not been at peace at all over the past 3 days. Over 30% have severe difficulty sharing their feelings and approximately 50% in each study arm report high levels of worry. More than 80% of participants report that they feel that their life is worthwhile.

5.2. Phase 2: Semi structured qualitative interviews

5.2.1. Sampling and sample characteristics

Participants were recruited to the qualitative phase of the study a minimum of one month and a maximum of 9 months after they had exited the quantitative phase of the study.

In terms of deviant case selection, there was only one participant who reported clinically significant deterioration, who also was alive at study exit. This participant was purposively included in the qualitative sample. The sample characteristics are described in Table 5-6 with reference to the

Results 1: Description of the data

sample for the entire TOPCare dataset used in the analysis of the quantitative data, to enable visual assessment comparability.

Table 5-6 Characteristics of sample for phase 1 and phase 2 of study

Variable	Phase 1 sample (n=120)	Phase 2 Sample (n=30)
Mean age (years, sd)	39.4 (8.7)	39.1 (6.9)
Gender (% female)	81%	80%
Partner status yes N (%)	76 (63%)	17 (56.7%)
Number of children Mean (sd) Median (IQR)	2.7 (2.1) 2 (1-4)	2.4 (1.4) 2 (2-3)
Number of financial dependents Mean (sd) Median (IQR)	3.9 (2.4) 3 (2-5)	3.2 (2.0) 3 (2-4)
Education attainment N (%)		
None	10 (8.3%)	3 (10.0%)
4 years or less	3 (2.5%)	2 (6.7%)
Primary education	76 (63.3%)	15 (50.0%)
Secondary education	27 (22.5%)	10 (33.3)
Diploma	4 (3.3%)	0 (0%)
CD4 count at baseline Mean (sd)	380 (222.89)	348.13 (273.75)
Receiving TB treatment? Yes n (%)	10 (8.3%)	5 (16.6%)
Received an AIDS diagnosis? Yes n (%)	119 (99.2%)	30 (100%)
Owens a bicycle? Yes n (%)	25 (20.8%)	8 (26.7%)
Owens a fridge? Yes n (%)	30 (25%)	7 (23.3%)
Owens a television? Yes n (%)	74 (61.7%)	18 (60%)
Owens a car? Yes n (%)	5 (4.2%)	2 (6.7%)
Owens a radio? Yes n (%)	76 (63.3%)	18 (60%)
Clinically significant improvement reported on MOS-HIV MHSS? Yes n (%)	62 (54.4%)	18 (60%)

Participants in the sub-sample phase 2 appear to be similar to the sample for phase 1 in terms of the clinical and demographic variables (Table 5-6). In order to describe levels of affluence within the dataset, in place of the distribution of poverty quintiles, which are somewhat abstract, the proportion owning a bicycle, fridge, television, car and radio are reported to demonstrate levels of

affluence in more concrete terms. These variables also demonstrate the similarity between the samples for phases 1 and 2 in terms of affluence. If experience of the study is associated with these clinical and demographic variables, this suggests that the variability of experience in the TOPCare sample should be captured within the sample for phase 2.

The mean length of the interviews was 41.6 minutes (sd 11.8), with a median time of 40 minutes (range 26 -76 minutes). They appear to be shorter in the intervention group compared with the control group, although the difference is very slight (38minutes v 41.5minutes).

5.2.2. Transcription and translation

One translator transcribed 16 of the 30 interviews, with the remainder translated by two other translators. All translators were selected first on the basis of experience of previous experience of interview translation and secondly on the basis of the quality of one translation they provided. After checking the manuscripts against the original recordings, minor adjustments for accuracy and comprehension were made by the researcher who conducted the interviews.

5.2.3. Coding framework

In the thematic analysis of qualitative data four major themes emerged: experience of healthcare, experience of research, living with HIV and sources of benefit. Experience of healthcare included data on interactions with healthcare staff outside of the study and the experience of medication management beyond ART. Experience of research encompassed participant descriptions of participation in the study, their understanding of the research and consent processes and descriptions of the content of the intervention. Living with HIV encompassed participant descriptions of aspects of their lives which were affected by their HIV positive diagnosis. Sources of benefit include participant descriptions of sources of therapeutic benefit from control and intervention study arms. They are depicted as active ingredients of the intervention, and therapeutic aspects of participation in the study. The coding framework is depicted and discussed more fully below in Figure 17, Figure 18, Figure 19, and Figure 20.

Figure 17 Coding Framework for 'Experience of healthcare'



Results 1: Description of the data

Experience of healthcare encompassed all data describing interactions with healthcare systems. This included participant experiences of medications (not including ART) for symptoms management etc. which they received in the course of receiving healthcare from the standard care clinic and other providers such as the Government hospital.

Figure 18 Coding Framework for 'Experience of research'

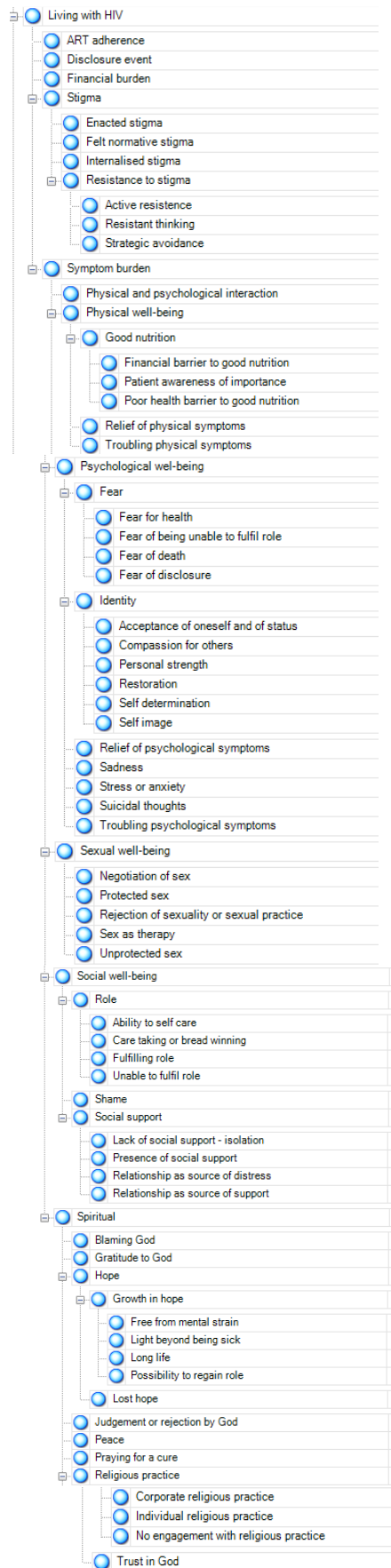


The theme of experience of research encompasses data on participant understanding of consent and the reasons they gave for consenting to participate in the trial. This was coded as it was realised that this was important to gain a deeper insight into the participant's understanding of the research process, which affected their perceptions of the actions of the study team. Participants sometimes misunderstood the practice of data collection as the researcher's personal interest in them, because they lacked previous experience of research (discussed in fuller length in Discussion section). This theme also encompassed data on the content of the intervention, and participant experience of interactions with the study team.

Living with HIV (Figure 19) was the largest major theme, containing data on the experience of life with HIV in Mombasa. The theme of 'Living with HIV' contained 5 sub-themes presented in Figure 19: ART adherence, disclosure event, stigma, symptom burden, and financial burden. The data coded at symptom burden and in the sub-themes of social and psychological well-being were examined and interrogated to address objective 3 as well as data coded under the theme of stigma, as stigma falls between the psychological and social domains, in that it influences and is influenced by both.

Results 1: Description of the data

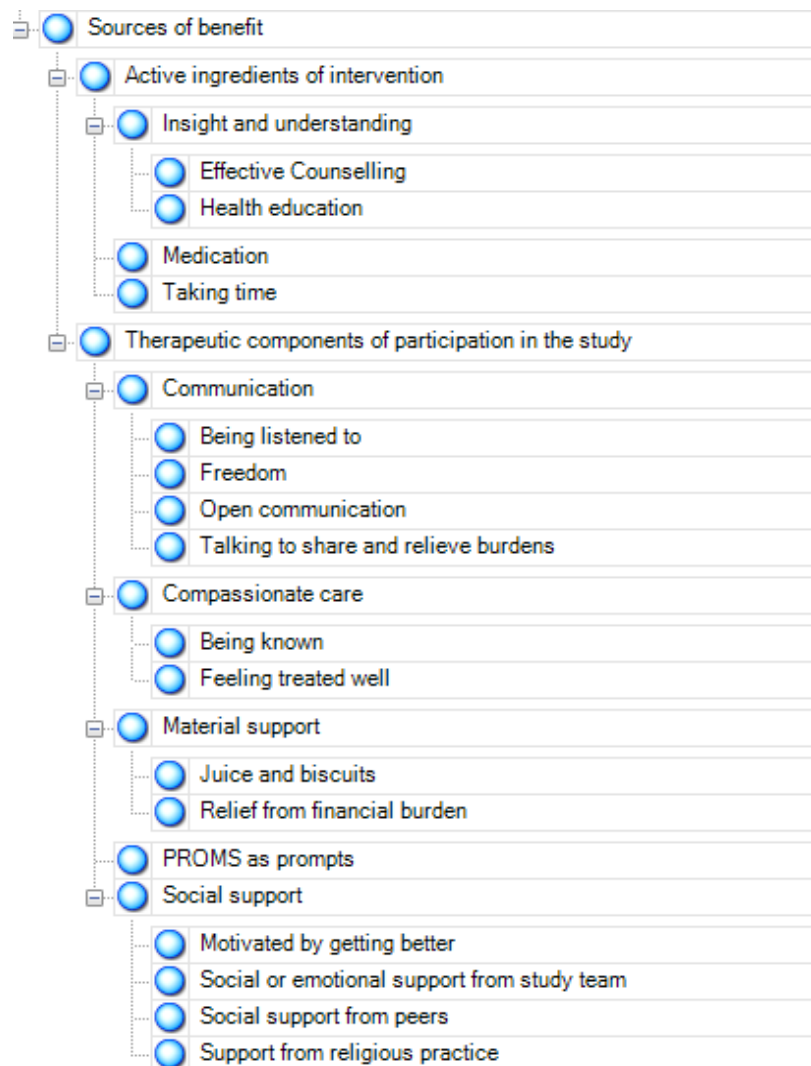
Figure 19 Coding framework for 'Living with HIV'



Results 1: Description of the data

Participants were asked about their views on what was the most therapeutic or beneficial aspect of the study. Their responses to this question and descriptions of why and how participants felt they had changed or improved during the study period, were coded at the major theme of 'Sources of benefit' (Figure 20). The sources of benefit are divided into active ingredients of the intervention and therapeutic aspects and processes of participation in the study.

Figure 20 Coding framework for 'Sources of benefit'



This data will be used to address objective 4, where the quantitative and qualitative data are analysed to explore and identify active ingredients and mechanisms of action of the intervention and therapeutic aspects and processes of study participation. A list of definitions of themes and sub-themes within the coding framework is included in Appendix 14.

6. Results 2: Results by objective

In this chapter I present the results of data analysis described in section 4.6 to meet the objectives of the study. These results are presented by objective and where relevant, according to study phase.

The chapter closes with a summary of all findings by objective

6.1. Objective 1

To determine baseline levels of mental well-being and to examine associations between baseline mental well-being and demographic and clinical characteristics among patients with HIV on ART enrolled in a randomised controlled trial (RCT) of a nurse-led palliative care intervention.

Baseline measures of mental health and well-being are reported below.

6.1.1. MHSS

The median MHSS score, inter-quartile range (IQR) and distribution for full sample and by study arm is presented in Figure 21 and Table 6-1. This represents a median score slightly below the reference population cited by the measure authors Wu *et al* (307). In the graph below, 0 is the worst possible score and 100 is the best possible score.

Figure 21 Distribution of MHSS at baseline for full sample and by study arm

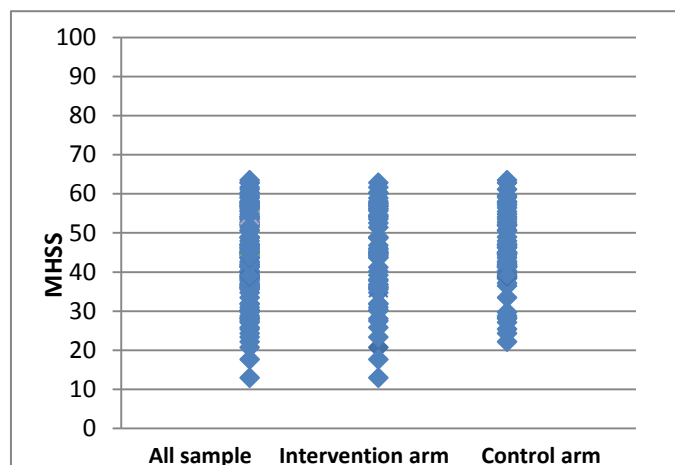


Table 6-1 Median and IQR MHSS at baseline for all sample and by study arm

Whole sample median MHSS (IQR)	Intervention median MHSS (IQR)	Control median (IQR)
44.8 (IQR 36.97-53.78).	44.8 (35.9-55.1)	44.7 (39.8-52.1)

Results 2: Results by objective

Bivariate analysis of MHSS with clinical and demographic variables at baseline is reported with test statistic, confidence intervals and p value (Appendix 15). This bivariate analysis identified an association between MHSS score and gender, CD4 count at baseline and age in years, using $p < 0.25$ as a threshold for significance. These variables were entered into the multivariate analysis. The residuals of the linear regression model were not normally distributed (Shapiro Wilk test $z = 6.70$ $p < 0.001$) therefore MHSS was categorised into 6 quantiles of 10 points, to perform enable logistic regression.

Table 6-2 Multivariate ordered logistic regression analysis to identify association between MHSS and independent variables at baseline (n=119)

Variable	Proportional log odds ratio (95% CI)	P value
Gender	0.31 (0.13,0.75)	0.01
Age in years	0.98 (0.94,1.02)	0.30
CD4 count at baseline	1.00 (1.00-1.00)	0.71

This model analysis identified an association between MHSS and gender. For women, the log odds of reporting better MHSS were 70% lower than that of men at baseline, holding CD4 count at baseline and age constant. Tests for the proportional odds assumption prove insignificant (χ^2 $p = 0.25$) suggesting that the assumptions are met.

Psychological quality of life as measured by MHSS was not associated with age, partner status, number of children, number of financial dependants, education, wealth, time since diagnosis, time on ART, CD4 count, and receipt of TB treatment in HIV positive patients on ART with moderate to severe pain or symptoms at baseline.

6.1.2. GHQ-12

The distribution of GHQ-12 score for the full sample and by study arm is reported in Figure 22 (best possible score 0, worst 12) and Table 6-3. In the literature a score of 4, 5 or 6 is used as a threshold above which the respondent is identified as having psychiatric morbidity, depending on the context and sample (316).

Results 2: Results by objective

Figure 22 Distribution of GHQ score at baseline for full sample and by study arm

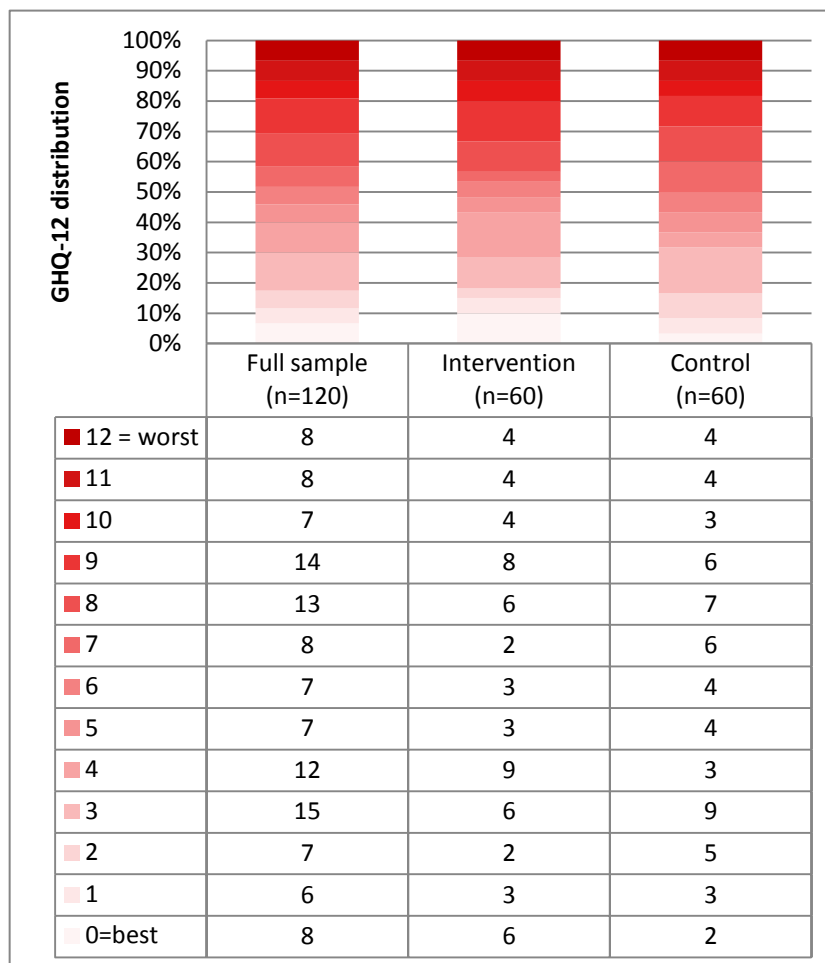


Table 6-3 Median and IQR GHQ-12 score for full sample and by study arm

Full sample median GHQ score (IQR)	Intervention median GHQ score (IQR)	Control median GHQ score (IQR)
6 (3-9)	6 (3-9)	6.5 (3-9)

Bivariate analyses of associations between GHQ-12 score and baseline demographic and clinical independent variables are reported in Appendix 15. The findings suggested some evidence for an association with GHQ identified psychiatric morbidity and older age in this sample ($p=0.02$). There were no further associations identified therefore no multivariate analysis was performed.

There was no evidence for an association between psychiatric morbidity and gender, partner status, number of children, number of financial dependents, education, wealth, time since HIV diagnosis, time on ART, CD4 count and receipt of TB treatment in HIV positive patients on ART reporting moderate to severe pain or symptoms.

6.1.3. APOS worry item

The distribution of the APOS worry item at baseline is presented in Figure 23 and Table 6-4. The bar chart shows that distribution of worry across the study arms was similar, with the majority of the sample either reporting that at baseline they were worried all of the time or not at all.

Figure 23 Distribution of APOS worry score at baseline for full sample and by study arm

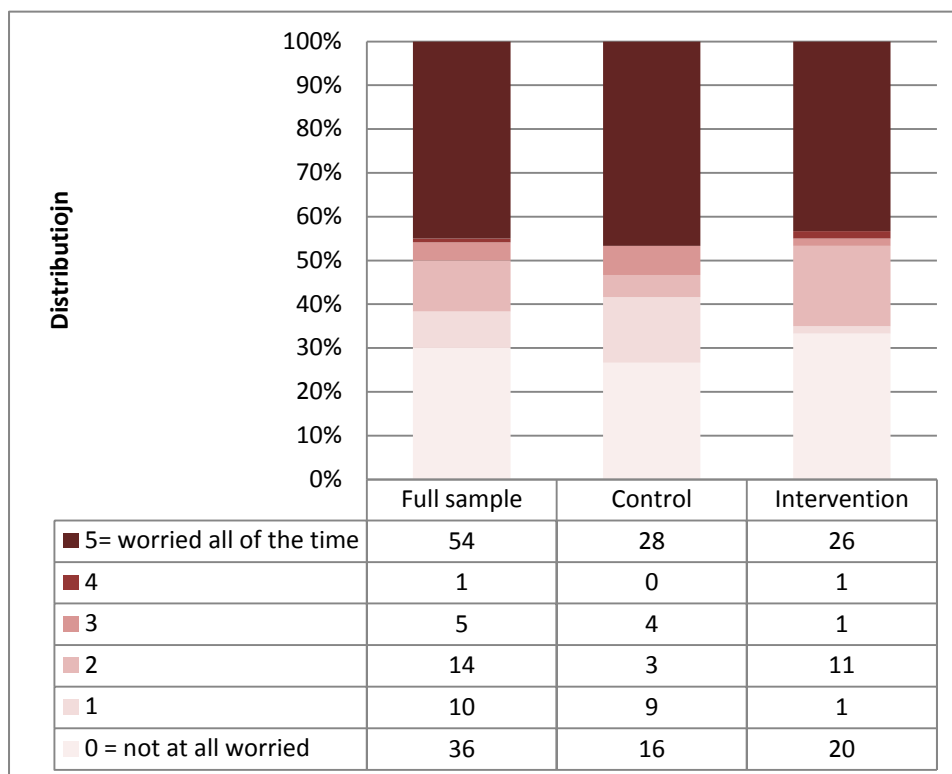


Table 6-4 Median and IQR of APOS worry item

Whole sample APOS worry median (IQR)	Intervention APOS worry median (IQR)	Control APOS worry median (IQR)
2.5 (0-5)	3 (0-5)	2 (0-5)

Details of the bivariate analysis can be found in Appendix 15. No associations were identified between worry and gender, age, partner status, number of children, number of financial dependants, education wealth, and time since HIV diagnosis, time on ART, receipt of TB treatment and CD4 count

6.1.4. APOS share item

The stacked bar chart presenting the distribution of APOS share item at baseline highlights considerable ceiling effect, with 53% reporting the highest possible score at baseline (Figure 24).

Results 2: Results by objective

Figure 24 Distribution of APOS share item at baseline for full sample and by study arm

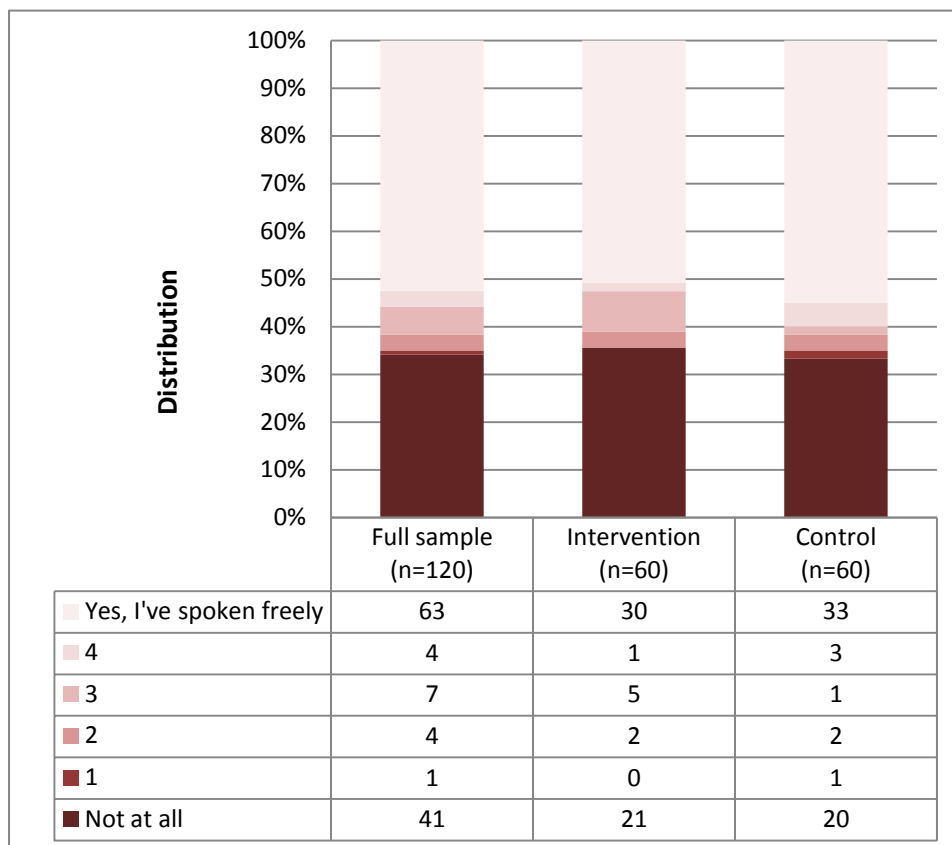


Table 6-5 Median and IQR of APOS share item at baseline for full sample and by study arm

Whole sample APOS share median (IQR)	Intervention APOS share median (IQR)	Control APOS share median (IQR)
5 (0-5)	4.5 (0-5)	5 (0-5)

Details of the bivariate analysis can be found in Appendix 15. No associations were identified between the ability to share feelings and gender, age, partner status, number of children, number of financial dependants, education wealth, and time since HIV diagnosis, time on ART, receipt of TB treatment and CD4 count.

6.1.5. Summary of findings from objective 1

The mean baseline MHSS was 44.8, lower than the reference group reported in the literature (307). MHSS was worse in women compared to men ($p=0.02$) at baseline. There was no evidence of an association between MHSS and age, partner status, number of children, number of financial dependants, education, wealth, time since HIV diagnosis, time on ART, CD4 count and receipt of TB treatment in HIV positive patients on ART reporting moderate to severe pain or symptoms.

Baseline GHQ score indicated some evidence of psychiatric morbidity in the sample, equally distributed between control and intervention study arms. There was also evidence for increasing

psychiatric morbidity with age ($p=0.02$). There was no evidence of any association between psychiatric morbidity and gender, partner status, number of children, number of financial dependents, education, wealth, time since HIV diagnosis, time on ART, CD4 count and receipt of TB treatment in HIV positive patients on ART reporting moderate to severe pain or symptoms.

Neither worry or the ability to share feelings were associated with age, gender, partner status, number of children, number of financial dependents, education, wealth, time since HIV diagnosis, time on ART, CD4 count and receipt of TB treatment in HIV positive patients on ART reporting moderate to severe pain or symptoms.

6.2. Objective 2

To identify any effect of the palliative care intervention on mental health and well-being, comparing participants receiving the intervention and standard best practice.

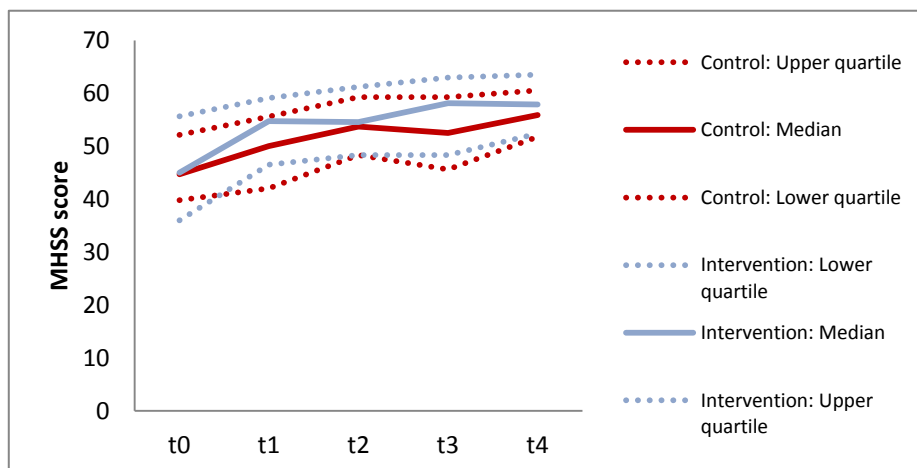
The data for the MOS-HIV MHSS, GHQ-12 and the APOS items is presented for visual assessment and familiarisation with the data and analysed at monthly time points to examine change over time, and using multilevel hierarchical regression model for repeated measures.

6.2.1. Graphical depiction over time and analysis at monthly time points

6.2.1.1. MHSS

Summary measures (median and IQR) were used to graphically display the MHSS data (Figure 25). The line graph shows that both the median of the control and intervention study arm increased over time. The intervention group reported earlier benefit at month 1, which attenuated at month 2 and increased at month 3. By the final time point, they appeared similar.

Figure 25 Median MHSS over time comparing study arms (n=114)



Results 2: Results by objective

Due to the interval nature of the MHSS variable, it was first analysed using linear regression. The residuals of each regression were however not normally distributed, therefore the data was analysed using the MHSS data divided into 3 categories, using ordered logistic regression. The results are displayed by monthly time point in Table 6-6 below.

Table 6-6 Regression coefficients for effect of study arm on MHSS score at monthly intervals throughout the study period adjusting for baseline MHSS score (n=114)

Time	Coefficient (95% CI)	p value
Baseline (n=120)	0.29 (-0.44-1.02)	0.44
Month 1 (n=119)	1.11 (0.35-1.86)	<0.01
Month 2 (n=117)	0.47 (-0.25-1.18)	0.20
Month 3 (n=114)	0.75 (0.02-1.49)	0.04
Month 4 (n=114)	0.74 (-0.03-1.51)	0.06

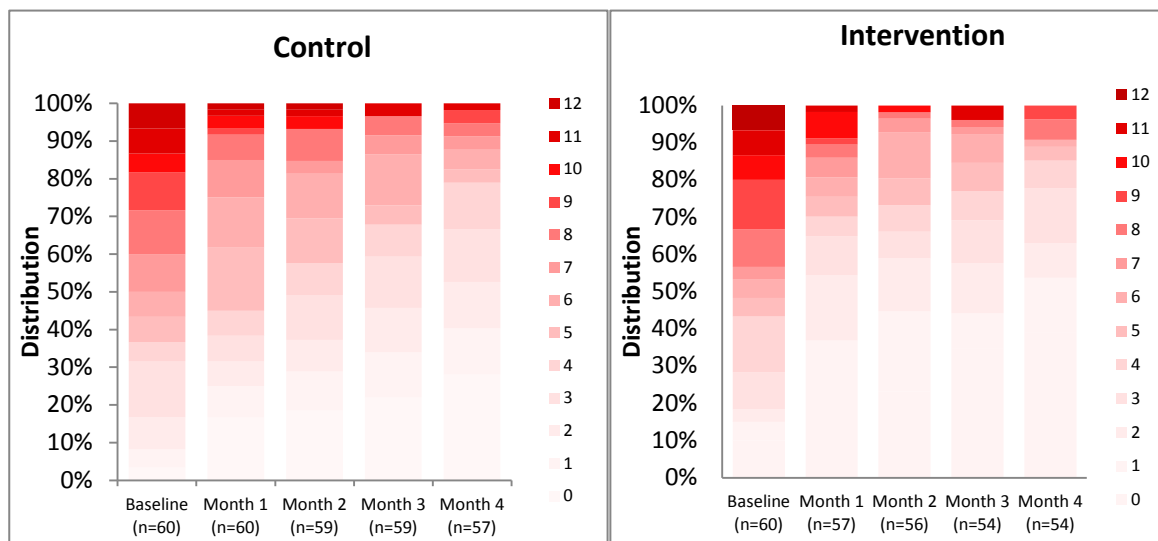
Monthly time point analysis of the MHSS data showed statistically significant difference between control and intervention study arm at month 1 and some evidence of a statistically significant difference at months 3 and 4, with benefit in the intervention arm.

6.2.1.2. GHQ-12

The distribution of GHQ-12 scores (12 point scale) are presented over time in bar charts and by study arm (Figure 26). Visual assessment suggested improvement in psychiatric morbidity in both study arms over the study period. As for the MHSS data, the intervention group improved more rapidly initially, with the initial difference between study arms attenuating over time. A low GHQ-12 score indicates an absence of psychiatric morbidity.

Results 2: Results by objective

Figure 26 GHQ-12 score over time comparing study arms (n=114)



The GHQ-12 data were analysed in a multivariate model for each monthly time point, for effect of study arm on GHQ score. The data for GHQ-12 were found to violate the proportional odds assumption of ordered logistic regression, and therefore scores were divided into three categories, which preserved the assumptions. The model adjusts for baseline score (Table 6-7).

Table 6-7 Ordered logistic regression for effect of study arm on GHQ score at monthly intervals throughout the study period, adjusting for baseline score (n=114)

Time	Coefficient (95% CI)	p value
Baseline (n=120)	-0.18 (-0.86 to -0.51)	0.61
Month 1 (n=119)	-0.85 (-1.54 to -0.15)	0.02
Month 2 (n=117)	-0.84 (-1.56 to -0.13)	0.02
Month 3 (n=114)	-0.58 (-0.30 to -0.14)	0.12
Month 4 (n=114)	-0.51 (-1.25 to -0.23)	0.17

The analysis demonstrated a statistically significant difference between control and intervention at months 1 and 2, with benefit to the intervention arm.

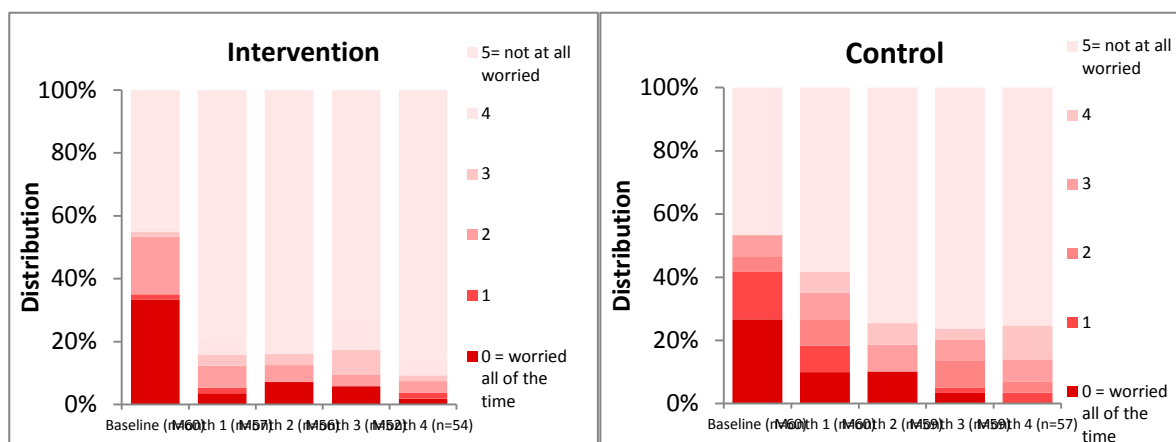
6.2.1.3. APOS worry

The distribution of worry score over time shows a similar pattern of decreasing worry over time in both study arms, with a more rapid decrease suggested in participants from receiving the

Results 2: Results by objective

intervention care package. Scores have been reversed from original scoring for this graphical depiction to facilitate comparison with the other APOS item (ability to share).

Figure 27 Distribution of APOS worry over time comparing study arms



The APOS worry data were then analysed using ordered logistic regression, adjusting for baseline score.

Table 6-8 Results of ordered logistic regression for effect of study arm on APOS worry score at monthly intervals throughout the study period, adjusting for baseline score (n=114)

Time	Coefficient (95% CI)	p value
Baseline (n=120)	0.13 (-0.53-0.79)	0.69
Month 1 (n=119)	-1.07 (-1.87- -0.26)	0.01
Month 2 (n=117)	-0.54 (-1.47- 0.39)	0.25
Month 3 (n=114)	0.00 (-0.86-0.87)	0.99
Month 4 (n=114)	-0.78 (-1.75-0.20)	0.12

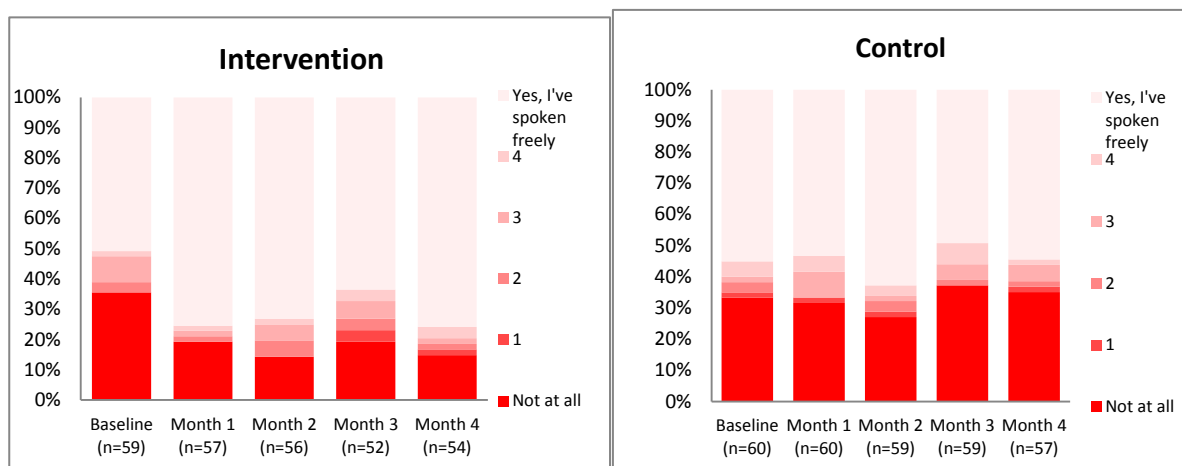
Monthly time point analysis showed a statistically significant difference at month 1 with benefit to the intervention arm, which attenuated and does not re-emerge at any subsequent time point.

Assumptions of the analysis were not violated at any monthly time point.

6.2.1.4. APOS share

The distribution of scores over time for APOS share suggested an immediate improvement in the intervention study arm from baseline, which was not seen in the control study arm (Figure 28).

Figure 28 Distribution of APOS share over time comparing study arms (n=109)



Once the improvement was made, most participants continued to report high levels of ability to share feelings in the intervention arm. The distribution appears to change little over time in the control study arm data. Data distribution suggestive of a ceiling effect is maintained over time in both study arms.

The APOS share data were then analysed using ordered logistic regression, adjusting for baseline score.

Table 6-9 Results of ordered logistic regression for effect of study arm on APOS share data at monthly intervals throughout the study period adjusting for baseline score

Time	Coefficient (95% CI)	p value
Baseline (n=120)	-0.15 (-0.84-0.53)	0.66
Month 1 (n=119)	0.92 (0.14-1.70)	0.02
Month 2 (n=117)	0.65 (-0.14-1.43)	0.11
Month 3 (n=114)	0.64 (-0.09-1.37)	0.09
Month 4 (n=114)	1.16 (0.35-1.97)	<0.01

The results of the analysis demonstrated a statistically significant difference between control and intervention study arm at month one and month four. Assumptions of the analysis were not violated at any monthly time point.

6.2.2. Analysis of repeated measures

This analysis was performed to assess for effect of study arm, whilst taking into account potential data clustering by participant and baseline score. Initially analysis using GEE was performed, but the residuals of each regression were found to be not normally distributed, and therefore the results were invalid.

GLLAMM was then performed, as a more robust technique with fewer assumptions for ordinal data. Each dependent variable was reduced to 4 quantiles to facilitate this analysis, which was performed using 8 quadrature points, a binomial distribution, the ordinal logistic regression link function (ologit) and correlation by participant. The ICC was also reported, indicating the degree to which the repeated measures were found to be clustered by patient (higher score indicates increased clustering).

Table 6-10 GLLAMM for effect of study arm on mental health and well-being, adjusting for baseline score

	Co-efficient (95% CI)	p value	ICC (95% CI)
MHSS (4 categories)	0.59 (0.12-1.07)	0.015	0.45 (0.36-0.54)
GHQ-12 (4 categories)	-0.50 (-0.96 to -0.03)	0.035	0.34 (0.25-0.43)
APOS worry (4 categories)	-0.38 (-0.87-0.11)	0.13	0.25 (0.17-0.34)
APOS share (4 categories)	0.92 (0.28-1.56)	0.005	0.31 (0.22-0.40)

This model indicated that participants allocated to the intervention study arm reported higher MHSS, reduced GHQ 12, and increased APOS share in the ordered log odds scale. No statistically significant difference was identified for APOS worry comparing intervention and control study arms.

There was a statistically significant difference between the control and intervention arm, with respect to longitudinally analysis adjusting for data clustering, in terms of psychological quality of life (MHSS) psychiatric morbidity (GHQ-12) and the ability to share feelings (APOS share), but not for worry (APOS worry), with benefit to the intervention.

6.2.3. Null hypothesis

The null hypothesis for psychological quality of life (MHSS) is stated below:

There will be no difference in psychological quality of life, measured by the MOS-HIV MHSS, in longitudinal analysis of difference between participants allocated to receive the intervention (nurse led HIV palliative care) and participants allocated to receive the control (standard HIV clinic care)

Longitudinal analysis showed a statistically significant increase ($p=0.015$) in MHSS in participants allocated to receive the intervention care package, thus the null hypothesis is rejected.

6.2.4. Summary of findings from objective 2

Analysis by monthly time point indicated statistically significant difference between study arms at month one for psychological quality of life (MHSS), psychiatric morbidity (GHQ-12), worry and ability to share, with benefit in the intervention arm. At month two the difference persisted for psychiatric morbidity, but for no other outcomes. At month three there was benefit in the intervention arm for psychological quality of life but no other outcomes, and at the final time point there was statistical evidence for benefit in the intervention arm for the ability to share feelings.

Analysis of repeated measures identified a statistically significant difference between control and intervention groups in terms of psychological quality of life, psychiatric morbidity and the ability to share feelings, but not for worry. The difference indicated benefit for the intervention arm for each outcome. The null hypothesis of no effect was rejected.

6.3. Objective 3

To determine and describe participant experience and longitudinal response to participation in the study in terms of psychological and social well-being, and to identify and explore associations between participant response and demographic and clinical characteristics

Results of the quantitative analysis of phase 1 data will be presented first, followed by qualitative result of analysis of phase 2 data, ending with an integrated summary of the combined findings.

6.3.1. Phase 1 data analysis of response to participation

To identify which variables, in addition to study arm, had an effect on participants' mental well-being area under the curve analysis was performed to examine association with demographic and clinical independent variables (see 4.6.5.1).

6.3.1.1. Area under the curve

Area under the curve analysis is a longitudinal summary of the measurements for each individual participant. To decide whether the data is of adequate quality for the trapezoid method, the time between data collection appointments was analysed (Table 6-11).

Table 6-11 Summary of time in between data collection appointments (n=112)

Time interval	Mean (days)	sd
Time between T0and T1	29.2	5.1
Time between T1 and T2	28.1	10.7
Time between T2 and T3	30.6	10.8
Time between T3 and T4	29.8	4.8

Appointments were quite evenly spaced and therefore the trapezoid method could be used to calculate the AUC.

6.3.1.2. AUC Distribution

The AUC distribution for the MHSS suggested an almost normal distribution of results, with a slight negative skew. The distribution of the GHQ-12 AUC data was skewed positively, indicating less psychiatric morbidity over the study period.

Results 2: Results by objective

Figure 29 Distribution of MHSS AUC data (n=114) Figure 30 Distribution of GHQ-21 AUC data (n=114)

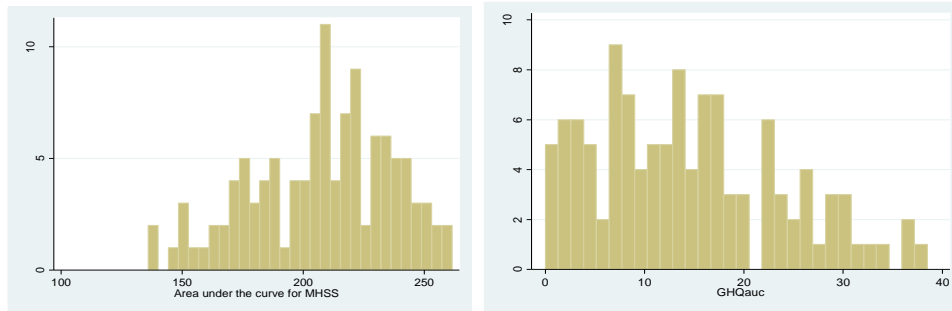
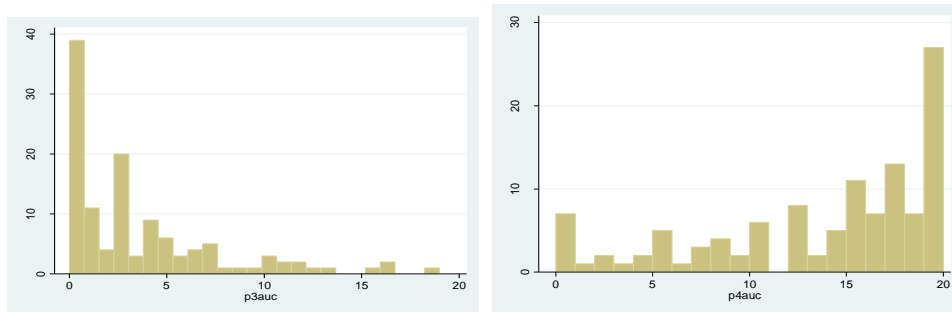


Figure 31 Distribution of APOS worry AUC data (n=114) Figure 32 Distribution of APOS share AUC data (n=114)



The APOS worry AUC data was positively skewed. As a low score indicated fewer problems in this item, this positive skew showed the low level of worry over the study period. The APOS share data was negatively skewed. This item was scored in the reverse, where a high score indicated fewer problems, thus this distribution indicated high levels of ability to share.

6.3.1.3. Association with demographic and clinical independent variables

MHSS AUC

The results of the multivariate linear regression are reported in Table 6-12. No Bonferroni correction was necessary as 4 variables were entered into the model, which meant there were 30 respondents per variable. The residuals for this regression model were normally distributed (Shapiro Wilk $z=0.87$ $p=0.19$).

Table 6-12 Results of multivariate linear regression model of MHSS AUC and independent variables (n=114)

Variable	Regression coefficient (CI)	p value
Study arm	9.26 (2.18-16.33)	0.011
Baseline MHSS score	2.03 (1.70-2.36)	<0.001
Poverty quintile	-3.57 (-6.13- -1.02)	0.007
Educational attainment	-3.77 (-8.17- 0.58)	0.089

Results 2: Results by objective

The adjusted r^2 for this model was 58% indicating that study arm, poverty, educational attainment and baseline score account for 58% of the variability in MHSS AUC. Allocation to the intervention group was associated with an increase of 9.26 AUC points, holding baseline score, poverty and education constant. Each increase of baseline score was associated with an average increase of 2.03 MHSS AUC holding study arm, poverty and education constant.

For each increase in poverty quintile, there was an associated 3.57 points decrease in MHSS AUC. This suggested that an increase in poverty was associated with decrease in psychological quality of life, holding study arm, baseline score and education constant.

For every increase in educational attainment, there appeared to be a corresponding 3.77 decrease in MHSS AUC, indicating that higher educational attainment was associated with poorer psychological quality of life, holding study arm and wealth constant. This finding has marginal evidence for statistical significance.

These findings suggested a significant predictive relationship between improved psychological quality of life and people who are richer, less educated and allocated to the intervention study arm.

GHQ-12 AUC

The residuals for a simple regression model were not normally distributed (Shapiro wilk test $z=1.69$, $p=0.05$), so this analysis was performed using ordered logistic regression, dividing GHQ AUC into 10 categories. The test for the proportional odds assumption indicates that this assumption had not been violated ($X^2 18.65$ $p=0.77$).

Table 6-13 Results of multivariate ordered logistic regression model for GHQ-12 AUC category and independent variables (n=114)

Variable	Coefficient (95% CI)	p value
Study arm	-0.88 (-1.55- -0.21)	0.010
Baseline GHQ-12 score	0.35 (0.24-0.46)	<0.001
Poverty quintile	0.24 (0.001-0.47)	0.041

Allocation to the intervention study arm was associated with a decrease of 0.88 in AUC ordinal category, or reduced psychiatric morbidity over time in the intervention group ($p=0.01$). For every unit increase in baseline score, GHQ-12 AUC category increased by 0.35, when study arm and wealth

are held constant ($p < 0.001$). This suggested that those who began with increased morbidity did less well over the study period. For each increase in poverty quintile, GHQ-12 AUC category increased by 0.24 categories, indicating that increased poverty was associated with increased psychiatric morbidity holding study arm and baseline score constant.

APOS worry AUC

Analysis of the APOS worry item AUC showed that the assumptions of both linear regression and ordinal logistic regression were not met, as the residuals of linear regression were not normally distributed, and the assumption of proportional odds was violated. Multinomial analysis was attempted but the results of this failed to report any trends or findings of any coherence. Therefore AUC worry data could not reasonably be analysed and this data will not be reported.

APOS share AUC

The APOS share AUC data was analysed using ordered logistic regression because in the preliminary regression models, residuals of a linear regression model were not normally distributed ($z = 5.94$, $p < 0.001$). The assumptions of ordered logistic regression were violated when this data was divided into 10 quantiles, but not when divided into 4, therefore 4 quantiles of APOS share AUC data were used ($\chi^2 = 145.59$ $p = 0.06$).

Table 6-14 Multivariate ordered logistic regression model of APOS share AUC and independent variables (n=114)

Variable	Coefficient (95% CI)	p value
Study arm	-0.85 (-0.18-1.53)	0.013
Baseline APOS share score	0.44 (0.28-0.60)	<0.001
Gender	-0.91 (-1.79- -0.04)	0.040
Highest educational attainment	-0.59 (-1.01- -0.18)	0.005

There was strong statistical evidence that allocation to the intervention arm ($p = 0.01$) and higher baseline score ($p < 0.001$) were associated with improvements in ability to share over the study period. Female gender ($p = 0.04$) and increasing educational level ($p = 0.005$) were associated with a decreased ability to share over time, adjusting for allocation to study arm and baseline score.

This suggests that those in the intervention study arm, those who began with higher ability, men and participants with lower education level reported increased ability to share during the study.

6.3.1.4. Summary of quantitative longitudinal response analysis

The results of the quantitative analysis for association of outcomes with demographic and clinical variables show that over time, adjusting for the effect of study arm and baseline score:

- Increased poverty was associated with worse psychological quality of life ($p<0.01$) and increased psychiatric morbidity ($p=0.05$).
- Increased educational attainment was associated with worse psychological quality of life ($p=0.04$) and ability to share ($p<0.01$).
- Male gender was associated with increased ability to share ($P=0.04$).
- Increased psychological quality of life and ability to share and decreased psychiatric morbidity were all associated with allocation to the intervention study arm (all $p=0.01$).
- Finally, better health status in terms of psychological quality of life, psychiatric morbidity and ability to share at baseline were associated with improvement in status over the study period ($p<0.001$ for all). This suggested that those who began the study with better mental health and well-being, reported consistently better scores over time, adjusted for study arm and other variables. In conclusion, baseline score was the strongest, most consistent predictor of outcome.

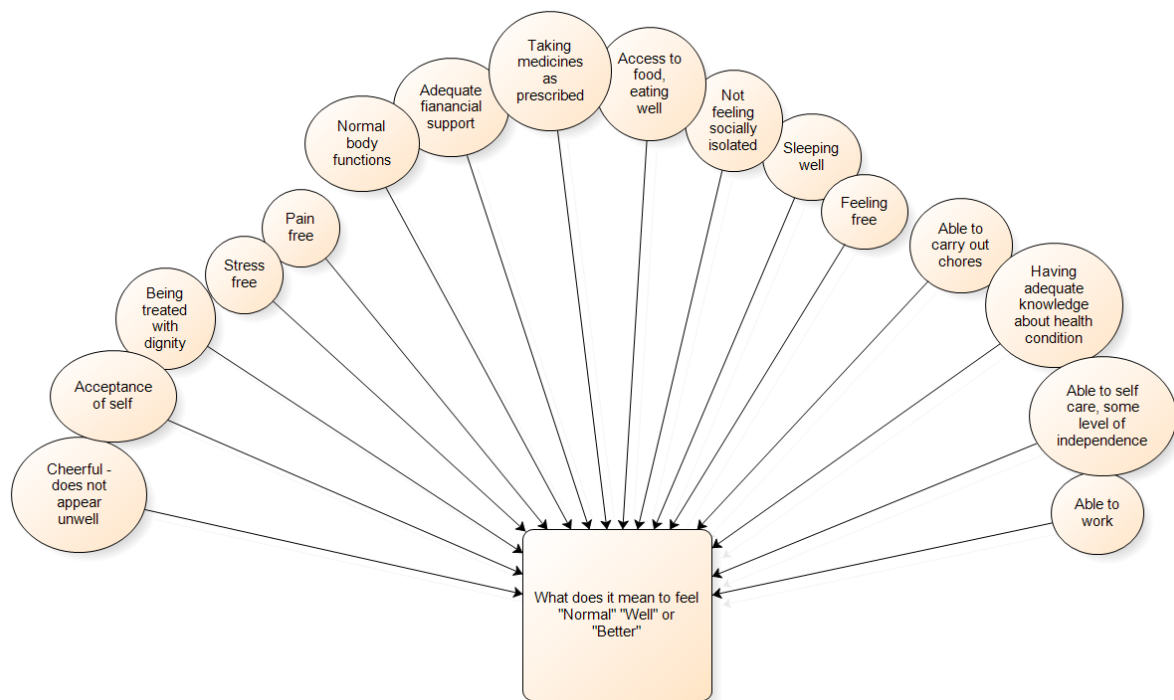
6.3.2. Phase 2 data analysis of response to participation

6.3.2.1. Cultural understanding of the concept of well-being

The model which was constructed from the participants' words and phrases used to describe what it meant to be normal, well or better, is presented in Figure 33.

Results 2: Results by objective

Figure 33 Participants cultural understanding of the concept of well-being



This model includes participants descriptions of what ‘well’ people are able to do, how they appear and how they are treated by others in society. The model identifies a variety of different aspects of well-being, and highlights participant’s emphasis on physical and social function in their understanding of what it means to be well. Among the most often repeated aspects were the ability to eat well and the ability to work, which may be related.

To address objective 3, (determine and describe participant experience and longitudinal response to participation), the qualitative data is reported according to the time period referred to by participants (before, during or after the study), and by study arm.

The majority of participants for phase 2 of the study reported clinical benefit in the quantitative outcome measures (Table 6-15). Amongst those who did not report clinical benefit there are those who reported some positive or negative change but not to a clinically significant extent (10 point change (307)). Only one participant, in the intervention group, reported clinically significant deterioration and remained alive at the end of the trial.

The findings of the qualitative data analysis will be presented for both study arms before the study began, with separation by study arm and report of clinically significant benefit during and after the study (Table 6-15).

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Table 6-15 Number and ID of participant with clinically significant benefit as measured by MHSS by study arm

		Clinically significant deterioration (MHSS)	No clinical benefit (MHSS)	Clinical benefit (MHSS)
Control (n=10)	ID number	(n=0)	097, 133, 156, 159 (n=4)	77, 107, 130, 143, 157, 158, (n=6)
Intervention (n=20)	ID number	124 (n=1)	108, 123, 139, 147, 154 (n=5)	075, 106, 110, 114, 119, 120, 125, 126, 129, 132, 134, 135, 138, 144 (n=14)

6.3.2.2. At entry to the study

This section provides an overview of the mental health and well-being of the entire sample at recruitment and entry into the study, as reported by participants at their exit interviews.

Twenty-four participants reported that they experienced fear in their lives before recruitment to the study; mostly fear of death and deteriorating health. Many thought that once diagnosed with HIV, deterioration and death was a certainty, and probably imminent:

I just used to think that the next thing was death; that is what I believed. I just used to see that I will just die because I had pains everywhere; I wasn't healthy. ID 075, female, 42 years, intervention

Few knew others who had lived with HIV for a long time in the community, perhaps because of the relatively recent advent of widespread availability to ART:

So I was in a depressive mood, because people always talked about the disease saying that one would have to die. ID 110, female, 28 years, intervention

Participants described anxiety because they assumed that it was impossible to get better and live normally as a HIV positive person:

Interviewer: What did you fear most about your life?

Patient: I was not sure if by using the drugs I could get helped and be able to live my normal life. ID 107, female, 46 years, control

Fears were associated with a lack of knowledge about the medication, and a lack of trust that it would be effective, sometimes based on experience of persistent complaints:

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I could go to the doctor and I'd be told to take this medication. I'd take until completion and still no difference. I even started reasoning, "If I'm being given medication and I'm not improving even after completing the dose, what could be happening – will I really get well?" Then I got ... I started getting worried. ID 107, female, 46 years, control

One time it's headache, the other time it's the stomach, then cold or is it malaria, I mean I was ever in poor health and I thought I'd go any time, never hoped of getting better. I never had a focused mind, I was very worried, because I wasn't used to this – coughing then this and that and then that and all these were upon me and I'd never been used to this. ID 125, female, 30 years, intervention

They reported receiving little encouragement from health care providers and others in their community, often reporting a lack of hope for the future. This lack of information, hope and trust in the therapeutic options led to fear and isolation:

I mean that state of feeling you've no hope of life and you think you are soon passing away....It's feeling that you are weighed down with too many thoughts because you don't have anyone to give a helping hand. ID 144, male, 32 years, intervention

Participants also reported a fear of disclosure, associated with the fear that they might be shamed, socially isolated or discriminated against due to their HIV positive diagnosis:

Initially, I had a lot of [hesitates] ... friends but when I knew about my status I started fearing them – because I feared they [hesitates] might be discussing about me. So I started fearing them. ID 110, female, 28 years, intervention

I was worried that if I told him the truth then, he would be shocked and ask, "Mum where have you contracted this disease and Daddy is not alive?" so that got me so worried. ID 126, female, 54 years, intervention

Participants reported telling family and friends that they had TB, to explain weight-loss and obvious ill health, but to avoid people gossiping. Secrecy was seen as the price for good relationships with the community:

[In the community] we related well, because, you know, whatever issues you may have in your heart remain your secret. And there is no need of spilling them over to everyone for no reason. ID 125, female, 30 years, intervention

Patients often saw themselves as shamed: disliking themselves as a person, feeling unworthy, or not normal:

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I was feeling isolated and I hated myself so much, I considered myself valueless and I felt like dying. ID 135, female, 50 years, intervention

Diagnosis with HIV was experienced as shameful, due to the socio-cultural associations of HIV with immorality and the associated stigma in this culture:

I was so afraid because in my entire life I never thought this disease would get me, I knew it was meant for some people with immoral behaviours within the community and I was living a straight, upright life even without a degree education. ID158, female, 33 years, control

Although she does not articulate exactly what she is afraid of, it is clear that this participant is experiencing an identity dissonance which has created fear. Participants also experienced stigma in the form of open blaming and shaming from their families. One participant reported how her brother had blamed her when she disclosed her HIV status, and described the associations of HIV with immorality:

[He said] you went and took your own illness. I told [you about] your husband, leave him, he will infect you with that illness; he likes a lot of women, now you see? Now you see? ID 133, female, 40 years, control

Participants also often blamed themselves for their diagnosis, expressing shame and guilt. They expressed feeling abandoned by God, blaming God, but most often feeling shamed by the punitive purity codes associated with conservative religious practice:

I felt guilty and responsible for my sickness so I felt like even if I cry to God he will never listen to me, but it wasn't so. Many people are positive and it is God who made it so. ID 139, female, 42 years, intervention

Once HIV serostatus had been disclosed, this sometimes led to the experience of discrimination and the exacerbation of the fears of participants who had not disclosed. One participant described how this stigma affected her economic activity and ruined her business selling cakes by the road:

They would say, "Hey, never buy buns from the lady with AIDS". So I couldn't do anything, I couldn't sell anything – nobody would come to buy them. ID 143, female, 36 years, control.

Experiencing this discriminatory behaviour or enacted stigma sometimes discouraged participants from disclosing their status, which led to increased isolation and suffering. Social isolation was a major cause of sadness; friends from before participants were sick had left, increasing their sense of vulnerability and isolation:

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The way they used to talk about me, that I have this illness, and then they started isolating me. At first we were together but when they knew I had that illness they started isolating me and that brought on the thoughts. When I look around, I can't find any companion. ID 133, female, 40 years, control

Some more specifically reported a lack of support in decision making and in managing their responsibilities, which highlighted their sense of isolation from the community:

Let's say, for instance, you need to eat but you don't have the food. You look around and you don't have anyone to help you. So you begin to lose ... [hesitates] you feel hopeless. ID 157, female, 48 year, control

The lack of opportunity, or difficulties in securing income meant there was a lack of money to buy food, and therefore neither they nor their families would be able to eat well.

Financial pressure was another oft-reported source of fear or anxiety. Participants worried about their ability to meet the needs of those who depended on them, both now and in the future.

Inability to fulfil their social roles in supporting their families or dependents, such as care taking or paid employment was perceived as shameful:

Mostly, the children used to cause me distress, particularly the one who is in standard 8. Due to being constantly in poor health, I was wondering whether I would be able or in good health again to educate my children. ID 106, female, 39 years, intervention

Physical illness was also cited as a cause of shame, sadness and anxiety. Participants described sadness due to the constant burden of being ill and in pain, at seeing their children sick because they too were HIV positive and shame at the indignity of being physically cared for when incapacitated.

The indignity for one woman was particularly painful:

I thought ... these boys are bathing me and they see me totally undressed, of course, your heart, you persevere, but in your heart it hurts, it agonizes. ID 133, female, 40 years, control

Some participants reported instances of social support after they disclosed their status, for example the woman quoted above described how difficult she found it to receive support from a family member, who cared for her when she was extremely sick. Often a young girl from the participant's extended family would be sent to help with cooking, drawing water and cleaning clothes.

Regardless of symptoms, belief in the inevitability and imminence of death was commonly expressed by participants and was described as a prevalent view in the community. Five participants from the total of 30 that we interviewed reported that before the study began, they had experienced suicidal

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ideation, either passively through giving up and fading away, or actively through suicide. Two of these participants were allocated to the control and three to the intervention study arm. They wanted to die because of their personal shame due to the discrimination they had experienced, stress due to ill health, suffering, financial pressures and out of a belief that there was no future for someone with a diagnosis of HIV:

I had a lot of stress that affected me a lot, I lost appetite, secondly I lost the morale of taking my drugs and I felt wise if I could just die. ID 077, male, 26 years, control

.... thinking back when I used to be so ill, I saw it wise to kill myself with a rat poison [laughing] mixing it with a glass of water and drink it all [laughing] that was the devil in me advising me to do so, because there was no need staying on earth surface in so much pain and suffering. At times I felt like hanging myself. ID 129, female, 43 years, intervention

There were few reported differences in the mental health and well-being between control and intervention study arms at baseline. A minority (n=4) did not report any problems with their mental health and wellbeing at baseline: 3 in the intervention arm and 1 in the control arm. Triangulation of mixed methods data however revealed that one woman, when asked about her emotional state at the start of the study reported that she had no concerns or reasons to feel depressed, but gave some indications of distress in the quantitative measures.

6.3.2.3. During the study

Participant experience of and response to participation in the study is now examined by report of clinical benefit measured by MHSS, and by control and intervention study arm. Participant explanations of their quantitative trajectories are integrated into this section of the results.

Intervention participants reporting clinically significant benefit

Intervention participants reported experiencing many processes of restoration or healing during the study. Receiving the intervention increased their understanding of HIV, and their understanding of how care affected self worth, which was an empowering and normalising experience:

Basically, through your counselling, as a matter of fact, without concealing anything, I really got helped. It picked me up from the ditch and placed me ... [hesitates] I mean it exhumed me and brought me back to the world, you see what I mean. ID 125, female, 30 years, intervention

Participants were encouraged by the study nurses to see themselves as normal, just like any other person, which improved self esteem and self image:

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It affected me because now I could do the things I was unable to do. I started feeling normal, and I started to like myself. All those things I never used to do. ID 135, female, 50 years, intervention

The concept of having HIV and being normal was clearly a strong message transmitted by the study nurses during the implementation of the intervention. It was often mentioned by participants during interviews, and was described as a powerful and significant message to receive:

I should laugh, eat, whatever am doing I should take it as normal and I will see myself as normal too. ID 126, female, 54 years, intervention

The participant quoted above contrasted the study nurse's belief and statement that it was 'normal' to be HIV positive, with being advised to 'behave normally' when she received her diagnosis, in case people realised that she was HIV positive.

Other participants described how their self-esteem, self worth and self acceptance were restored during receipt of the intervention, which positively affected their mental health and well-being:

I started viewing myself like any other person, as you see me now, like am not sick at all I stopped worrying about myself and focused. ID 129, female, 43 years, intervention

...now I can say, "Well, this is just an affliction but there are others who are worse. ... I'm encouraged that this is something I can manage. It's not like an accident or it's not like anything fatal that cannot be managed ... now I feel that there is a way I can deal with myself. I know that if this happens, I can do this and alleviate my pain, alleviate my sufferings and I can take charge – I feel now I can take charge of my life and the things that I do. ID 134, female, 41 years, intervention

I accepted myself, who I am and what I have in me. ID 138, female, 40 years, intervention

Participants often expressed their appreciation of being treated with respect and as equals by the study nurses, not as sick people:

Whenever I come in here and see you I feel very happy; I feel I have seen my friends; sisters; so am grateful. ID 075, female 42 years, intervention

The sisters were so good to me and I loved them just as they loved me. And this gave me a lot of freedom. ID 125, female 30 years, intervention

This respect encouraged trust to form between participants and the study team, and reinforced the participants tentative rejection of stigmatising societal messages they had received, for example

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messages that they were not worthy of equal treatment or inclusion in social activity. Participants grew in strength and confidence, and increasingly rejected stigma throughout the study:

Interviewer: and so after joining the study you stopped feeling shame and being stressed?

Interviewee: I don't even feel shame these days. ID 129, female 43, years, intervention

I'm no longer scared because when I came here, I was told I can have a long life. But when I was there [at the CCC] I felt worthless. ID 132, female, 45 years, intervention

Some used this increase in self confidence to disclose their status to their families for the first time, or to challenge family members who had excluded and isolated them due to their HIV diagnosis:

I was scared when I first started this study, and my health was also not in a good condition when I started, but as I came here for the discussions I started feeling ok, because I became free and started living my life as normal. And when I told my family about my health, they also joined hands in supporting me. ID 135, female, 50 years, intervention

Participants also described alleviation of anxiety and depression during the study. They described how guidance and support from the study team and the act of disclosing and discussing their concerns relieved the emotional burdens they had been carrying:

If you hadn't taught me and been open with me, I'm very sure that I'd have given up in life. Right now I'm okay. I'm okay sister. I can feel it. ID 138, female, 40 years, intervention.

Participants began to see themselves as normal, worthy of interest and care. This relief of anxiety coupled with effective medication reduced physical symptoms and enabled the participants to reflect on their situation and begin to have hope for their future:

Once the pain was off and ... when I used to come here, we would talk with you and you would ask me the questions and I'd reflect back. You know, I would go over my ... I'd reflect back, whatever that you had asked. ID 134, female, 41 years, intervention

Participants who had experienced suicidal ideation reported the alleviation of these symptoms due to the support of the study nurses:

[The study nurse] started advising me on how to control myself during such hard time. She told me to be reading the bible every time I feel like committing suicide, she even wrote a piece of bible verses to me and asked me to read them every now and then. Since then I have been so close to God and never had a bad thought again. I dumped the rat poison in a pit latrine. ID 129, female, 43 years, intervention

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Control participants reporting clinically significant benefit

Control arm participants described physical complaints which they experienced during the study, some of which were alleviated through care in the standard care clinic or elsewhere. The alleviation of these physical complaints improved their mental health and well-being, particularly when their ability to perform daily chores such as washing, cooking, carrying water or engaging in paid work were restored:

I can do laundry for someone and he pays me, something that I never used to do. I couldn't even take a bath on my own nor even eat, but right now I can light up my jiko [stove] and prepare a meal and eat on my own, it [participation in the study] has helped me a lot. ID 158, female, 33 years, control

Financial constraints continued to be challenging for participants during the study period. Temporary deterioration in psychological quality of life was attributed to financial constraints and the associated anxiety this caused. Participants had no money for the medication, and the food they needed to heal:

It is because of my life, considering that I have no money to take care of myself stressed me much. I felt apart because even if I could be using drugs they could not help much because I wasn't eating. And if the drugs weren't working then the graph had to curve down because all the stress and problems over burdened me. ID 130, female, 42 years, control

The reimbursement for transport given to each participant was used by many for medication, food or to support the family. This reportedly relieved some of the pressure associated with financial constraints:

I'd get prescription from there and sometimes if I came here I'd be given something like bus fare. That bus fare would really help me – using it for fare and I'd use like a 100 shillings on the prescription. I can say that I used to benefit. ID 107, 46 years, female, control

Behaviour change was reported, and attributed to increased awareness of the importance of support, protected sex, and strict adherence to medication. This was attributed to the persistent questioning from the researcher at the monthly data collection appointments.

After joining the study I became more careful, if someone would come and tell me I look smart, I would say thanks, but without condom no way Sir. Love me or not we can't have sex without condom because I know my own status so I control myself by using condom at my pleasure. ID 077, male, 26 years control

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Many participants reported an improvement in mental health and well-being during the study which they attributed to participation in the trial, and in particular to the warm and open approach of the study team:

Because the questions I was being asked and based on the reception I got, people were very free and they appreciated me – so that really encouraged me. ID 107, 46 years, female, control

I was ever sad, but when I joined the TOPCare study, everything started to resume to normal once again, because when I used to come here, everyone within the study was receiving me happily and this brought joy in my heart and I started being happy as well. ID 077, male, 26 years control

One participant in particular clearly articulated how, during the study, she began to realise the importance of sharing her concerns, and that she was not the only person experiencing HIV infection. This was a powerful experience for her, and she began to disclose her status to the people in the community:

Yeah and when I started, I was ... I just felt free because the first person I told my problem let me ... [hesitates] made me to realise that they also had a problem like mine... I set myself free, I came to realise what I was doing ... what I was thinking was wrong. Yeah after I came to realise that what I was doing was wrong, is when all the emotional problems ended. ID 143, female, 36 years, control

She went on to access effective medication from the clinic, which relieved her emotional and spiritual distress as well as her physical pain. She articulated how she realised that not being open about her status was destructive to her well-being, and how during the study, she grew in self awareness, and became more able to take care of her psychological and social needs:

I came to realise who I am and I got to know myself better, and I came to know where I was getting everything wrong. ID 143, female, 36 years, control

Increased openness among control arm participants also led to improved social well-being and a perception of increasing levels of social support within the community:

I was only close to my brother amongst my family members and because I wasn't open to him either, we never had a good relationship but during the study I changed. I could go to his house and explain my condition to him, care free. So our relationship has revived and we are free to each other. ID 158, female, 33 years, control

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Sometimes support from the family would be triggered by seeing others provide support. One family, which had previously ostracised their HIV-positive member, witnessed the support network which had been created by the community and, feeling shamed, became more supportive. Participants reported surprise at the support they had received from their family and friends. Finding others who were also positive was an enormous source of support for many participants:

What actually happened, from the day that I disclosed my status to my family and my friends, from that time, things started working for me – because they began supporting me, they began to be close to me and I found that we were the same and we were all sailing on the same boat. ID 143, female, 36 years, control.

Intervention participants reporting no clinically significant benefit

As described earlier, six intervention participants reported no clinical benefit as measured by the MHSS, of which one reported clinically significant deterioration.

When asked to explain why their quantitative trajectory reported deterioration in psychological quality of life, whether a temporary downward trend or an overall trend, all participants cited problems in other areas of their lives, such as unresolved physical pain, family and marital conflict, and financial pressures:

Interviewer: we see here during the fourth month that you went down so fast, what happened here?

Ahh! I had stress because my daughter had a wedding ahead and we had disagreements with my husband over the wedding I had to take all the responsibilities and include my family members to see if they could help me put things right, because I earn less at my place of work, so I was stressed. ID 139, female, 42 years, intervention

[My husband] caused me a lot of distress. Sometimes he beat me up. He would tell me that I'm the one who infected him with the disease. So I had a lot of troubles. That stress made me habitually ill. ID 147, female, 34 years, intervention

The illness I had in my stomach, when it starts to pain me, I lose appetite and since I don't eat well I lack strength and my health deteriorate. ID 124, female, 37 years, intervention

All participants did describe some therapeutic benefit from receipt of the intervention, which was sometimes captured as improvement in the quantitative outcomes, although not reaching clinical significance. Those who did report some benefit described how once their physical complaints had been addressed, things became easier psychologically, which led to an increased sense of well-being:

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You know once your body has relaxed your heart also settles down and subsequently everything gets restored. ID 123, male, 44 years, intervention

They described the emotional and social support they received from the study team and the comfort they found in realising they were not alone and isolated in their situation:

So when I come here we talk and by the time I leave this place, I feel a little bit relieved. I know as long as this thing is here – I come here, I see people lining up here and feel as if I'm not alone. So many people are suffering from this disease. ID 154, male, 32 years, intervention

Some participants reported partial restoration of positive identity, changing from seeing themselves as sick because of their HIV diagnosis to opening up to the possibility that they might be able to live with HIV. This involved some rejection of the concepts of being different to people who are HIV negative and the associated stigma:

When I came here, I started feeling peaceful; I started feeling like a human being. I was able to do anything, even lifting a bag of cement, anything, I could handle any job and I started feeling in my heart that I can do anything such that if I got a job any time I'd be alright. ID 123, male, 44 years, intervention

With the nurses, I have made me feel as if, though internally I know I'm HIV positive but on the other side I feel as if I'm no longer sick. I'm just like any other person out there who is not HIV positive because whenever I come here, I get my medicines. And I know if I take them as required I might have some more years to live. ID 154, male, 32 years, intervention

Only one participant reported a clinically significant deterioration. This woman reported that her lack of employment and financial constraints were extremely preoccupying, and the cause of any deterioration observed:

It was bad because I could...my mind could only think on how to get a job, how to get my daily meal and my life was just that way and I went on that way. ID 124, female, 37 years, intervention

She did however report that receiving the intervention was a positive experience for her, contrasting it with her experience in the standard care clinic, where they only give drugs and not time to talk:

When you go to the ordinary clinics there is no time. Ah sister will sit down with you and tell you this and this.....they only give you drugs or push you in to see the doctor, but when you come here you have to talk first, you have to discuss is when...she gives you drugs, you see its

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good when you come here because even if you have other ailment, the advice they will give you will make you feel much better. ID 124, female, 37 years, intervention

Perhaps because of the time spent talking and giving advice, she likened the experience of receiving the intervention to visiting the herbalist.

It was good because when you go to the sister or a herbalist, and then he/she tells you to follow the instructions and everything will be ok. It's obvious that you will leave that place feeling happy...so I used to leave this place feeling happy.

ID 124, female, 37 years, intervention

Control participants reporting no clinically significant benefit

In a similar way to the intervention participants who reported no clinically significant benefit, the control participant often reported severe stressors in their lives. Two participants reported unresolved physical pain, one reported experiencing what they described as a small stroke and one reported financial stressors and unemployment. No participants in the control arm reported a clinically significant deterioration as measured by the MHSS.

All participants reported appreciation for the study and benefit from participation. This was usually because being asked questions during research assessments conveyed a sense of care and attention, which prompted self-reflection and self care. Participants reported increasing in strength, self acceptance and understanding during the study:

Things were just ok, because I had understood and accepted myself as I am; I was never ashamed any more but rather very open. ID 97, male, 43 years, control

It changed, I was okay because when I came here you gave me advice we talked nicely and you give me faith.... when I leave here also I leave with strength. ID 133, female, 40 years control

The experience of answering questions appears to have been an intimate experience, which made participants feel valued.

It is because during my time in the TOPCare study, you used to ask me very important questions regarding my life and these are questions that I have never been asked before by any one since I tested positive, there is no one who have ever asked me how I feel nor how I live but when I came here you asked me all these. ID 159, female, 30 years, control

The researcher's interest in how the participants felt and how they lived was an important aspect of many participants' experience of the study.

6.3.2.4. After the study

Intervention participants reporting clinically significant benefit

Participants described how participating in the study had changed their outlook on life, reporting an increase in enthusiasm, hope, self esteem and self worth:

You guys, first and foremost changed my perception, to be precise. And then you taught me to take care of myself to live, plus, plus!The importance was my life. That is very important. The way you've taught me that life is more precious than the other stuff. ID 138, female, 40 years, intervention

Everything started to work out... because I used to view myself like unworthy [hesitates] ...but when I stopped thinking it was alright...I had peaceful nights and my days were always good. ID 126, female, 54, intervention

They described outward changes such as formalising relationships in marriage and joining a vocational training course in order to get a better job (ID 075), and beginning to make plans for the first time in years. One participant described accepting her mortality and planning her legacy for future generations of her family:

It's important because I'm doing fine – though nobody will live here on earth for ever – I will leave my grandchildren with a place of their own where they can live peacefully and always say, "Our grandmother built this place for us". ID 132, female, 45 years, intervention

Participants described improving in functional status, taking on work and providing for their families. This restoration of physical and social function was described as an important change for many participants:

Since I came here and started using medicines from here, everything has now improved – I'm now able to dust the floor and do everything else. I'm now well. I don't get sick as often, I'm able to feed well, and there is nothing, not even worries. I'm also able to do my work as usual. ID 114, female, 48 years, intervention

All of the participants in the intervention, who reported clinical benefit in the quantitative outcomes, described an appreciation of the study, which persisted after the study period.

However, some participants reported that the improvements they made whilst in the study did not persist. Worry, conflict at home and deterioration in physical health were cause for concern among the participants, as was no longer having access to effective analgesia:

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I began using your drugs my health has been good, but now that I am back to the other clinic I am back to my earlier situation.... It is not good, not like when I was here. ID 129, female, 43 years, intervention.

Participants reported that it was difficult to re-engage with the standard clinic. They had to wait to be seen, sometimes for a whole morning, which they found difficult after the minimal wait that they experienced when participating in the study. In addition, the volume of participants attending and the resulting time constraints meant that the interactions were necessarily shorter and focused on physical aspects of care. Participants reported that they felt more judged and less supported:

Because once I was at the C.C.C. [standard clinic] nobody used to take their time, sorry for saying but nobody used to take their time, umm, to teach you or at least to share with you your problems, you see. They just give you drugs and tell you after three months, come back. That's it. They hardly take their time. ID 138, female, 40 years, intervention

For instance if someone dwells on one issue, such as, "Do you feed properly?" I may not be feeding well but you are not giving me any help, you see? So if you ask me so and I tell you [they] say, "You don't feed well and if you are not careful might contract T.B again." So such things offend me. ID 125, female, 30 years, intervention

Other participants reported that they were able to communicate more confidently and openly with the staff in the standard care clinic, after the study had ended, articulating their problems and complaints:

Interviewer: You've said that you are now bold, that you can now tell the doctor that you need this or that. You can now speak for yourself, why have you gained that transformation?

Interviewee: It's attributed to the instructions I received here – the way you told me never to conceal anything to myself, that I should be open and never fail to report a sickness. ID 106, female 39 years, intervention

For some participants, specific changes, and the reasons why they experienced changes were less easy to identify:

They built me psychologically and influenced the way I thought about life. I started taking it in another way. ID 110, female, 28 years, intervention

I've become stronger, I'm more inspired, you see. Now I can take charge. I mean I don't seem to be very scared. You see ... I don't seem to be very scared now I can say, "Well, this is just an affliction but there are others who are worse". ID 134, female, 41 years, intervention

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It has changed my thought, cleared my mind and my feelings also, I felt like one who matters in the society.... it made my heart stronger and I proceeded on with my normal life. ID 135, female, 50 years, intervention

They reported that they felt more optimistic and that their overall way of thinking about themselves had changed.

Control participants reporting clinically significant benefit

Participants allocated to the control also reported an increase confidence and ability to be open about their status, which they attributed to participation in the study:

I came, I was received well, then we would be asked those questions but now I can see those questions and discussions have helped me - in the sense that if we were not having such forums, I wouldn't have been helped and again I wouldn't have had much freedom concerning my status. I would have continued to be timid. ID 107, female, 47 years, control

After the study, many reported increased social integration; as they felt better about themselves, they felt better about interacting with their friends and neighbours. Instead of hiding from visitors and isolating themselves, they welcomed the opportunity to interact as “normal”:

I am a happy person right now and I pay them visits as well, I also feel that they see me living as normal and doing my own work without fear. Unlike before, I never used to talk to anyone even if they would pay me a visit and that bored them from coming but everything is normal right now. ID 158, female, 33 years, control

They reported the alleviation of emotional burdens, such that there were no longer any problems. Some also reported return to their previous physical and social functional status, earning money and maintaining their household:

The good outcome is how I started doing my daily chores normally without any problem. I was doing my simple house chores and I was also doing my business of salonist as usual, I had good health not bad. ID 130, female, 42 years, control

In addition, fulfilling their social role, whether earning money or taking care of family members, was made easier by experiencing less worry, and worrying less enabled them to better fulfil the role:

It helped me because when you are not worried then you can attend to your responsibilities properly. You do your duties without any worries – working properly. ID 157, female, 48 years, control

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The participant who previously described the benefits of openness during the study grew in strength and courage. Although previously she had been forced to relocate her home and business due to stigmatisation and discrimination, she became more and more outspoken against the stigmatising views and discrimination she had experienced – rejecting them actively and openly. By the end of the study she was working as an activist in the community, dispelling myths that HIV was caused by witchcraft and identifying people in the community who had not been tested for HIV and bringing them to the hospital for testing.

Interviewer: And you are telling me this happened because of that time you were here with us?

Participant: Yeah, that gave me the courage even to stand in front of anyone to share with them about myself.... I have a very good relationship because I have disclosed my status to them. They have even nicknamed me – you know me as [ID 143] they call me a minister. And do you know it's a minister in charge of what? Minister for viruses! And I have accepted it.
ID 143, female, 36 years, control

Other participants in the control arm also took on activist roles after the study finished. In the case reported above, this was a new and socially approved role that she had taken on with much enthusiasm. Another participant was less public, but no less confident in her new role (N.B. TB is often used as a euphemism for HIV as co-infection is common and having TB is less stigmatising):

I visit a town clinic; where I normally go to take my drugs and when I get a new patient there, I call him sideways for a talk and advise him that T.B doesn't kill, if you take your drugs and eat well you will just recover. Then I would leave them with my number and later on, they would pay me a visit at my place just in case they had numerous questions to ask. I have realized that asking people questions in life helps them a lot, like it helped me, and I would also want to help people like I was helped. ID 158, female, 33 years, control

This participant experienced a restoration of positive identity, influenced by her physical status. She had felt psychologically and physically unwell for a long time, describing herself as if she wasn't a woman:

I was so sickling and I was 30 years by then but I could not experience my periods for almost one and a half years - I was just like a man. But after coming here everything changed to normal and I can now have my periods as normal and also regained my feelings back. ID 158 female, 33 years, control

Her participation in the study was a catalyst which enabled her to revert to what she saw as normality. However, confidence was not sustainable for some participants, who lost the ability to

Results 2: Results by objective

communicate openly when not explicitly given time to talk about their experiences or problems, when back in the standard care clinic:

I feel like I have reverted to the usual situation because there is very little to talk about when I go there – you only talk about your pain if you are in pain, you get your medicines. ID 157, female, 48 years, control

Intervention participants reporting no clinically significant benefit

Even though they reported no clinically significant benefit on the quantitative outcome measures, this group of participants expressed appreciation for the opportunity to be part of the study, and attributed participation with improvement in their holistic health and well-being:

You know after recovering from this numbness, I have been able to take care of myself. I can do anything and this has given me the peace of mind because I can now work and make an income. I can do a lot of things and if I called in for some work I can now go and work even if it's for a full week. I now feel that my body is fit such that I can now lift a 50 kilogram bag of cement. ID 123, male, 44 years, intervention

Participants report difficulty engaging with the standard care clinic compared to the study nurses. They reported being unable to report problems in the standard care clinic afterwards, because of a lack of trust that they could help them resolve their issues, despite attending the clinic over a period of many years.

I'm getting stressed again; reason being that he [husband] fights me all the time.... I felt that you are the ones who are capable of guiding me because even if I'd raise this issue with them ... whenever I'm completely down with stress I prefer coming to talk to you. ID 147, female, 34 years, intervention.

Participants cited a lack of time and inability to talk as a major barrier to creating a trusting therapeutic relationship with healthcare staff, which would enable them to disclose their concerns, and receive the support they required:

Because – when I go there, we don't have time to talk even though they are the same people I'm used to meeting every time. We don't have time to share, but when I come to this side, we talk, share and if I have any problem I raise it up. ID 154, male 32 years, intervention

Control participants reporting no clinically significant benefit

There were four control participants who did not report clinically significant benefit from the quantitative outcome measures, but all reported qualitative benefit or appreciation on some level due to participation in the study:

Results 2: Results by objective

I am so pleased with TOPCare because it gave me faith, courage and strength to convince myself that I am not alone in this struggle. We are many, and because some people hide their situations and die early I learnt to be open and bold. You always told me to just feel free. ID 97, male, 43 years, control

The financial reimbursement was also cited as a source of therapeutic benefit as it eased financial pressure in the family. For two participants, this and talking to the researcher were the most therapeutic aspects of the study. One participant described how he had grown in courage, which enabled him to interact with health care professional more directly. He described the difference between his interactions before the study and after:

I can't withhold any weird feeling in my body; I have to face the doctor directly without hesitation. ID 156, male, 40 years, control

Another participant describes the therapeutic process she experienced, in terms of self worth and hope for the future and the lasting impact of answering the questions of the researcher:

Before joining the TOPCare study I used to think a lot, but since I came here and you used to ask me questions I would go home and think deeply about them; then I would see and convince myself that there is life beyond being sick. Because when one contracts this disease, he feels unworthy and sometimes I used to see no sense in living on this earth, but when I used to come here for the sessions and you gave me questions that got me thinking, I saw light beyond just being sick. ID 159, female, 30 years, control

This extract articulates the transition many participants described or alluded to in terms of restoration of self worth and hope, and the way that participation in the study challenged their preconceived ideas about their self worth, associated with being diagnosed HIV positive.

6.3.2.5. Independent variables

In the quantitative findings, gender, education and wealth were associated with response to participation over the study period. The qualitative data from phase 2 was interrogated across these independent variables, looking at psychological symptoms and social problems over the study period.

Gender

In the quantitative findings, women had worse psychological quality of life at baseline, but men benefited more in terms of ability to share their feelings over the study period. Because of the lack of men in the sample who reported clinically significant benefit (n=1), comparison between those

Results 2: Results by objective

who reported benefit and those who didn't was not possible, so this analysis focused on the data for patterns in response between men and women over time.

Table 6-16 Number and IDs of participants with clinically significant benefit by gender and study arm

	Clinically significant benefit		No clinically significant benefit	
	Control	Intervention	Control	Intervention
Men (ID codes)	077 (n=1)		097, 156 (n=2)	123, 154 (n=2)
Women (ID codes)	107, 130, 143, 157, 158, (n=5)	075, 106, 110, 114, 119, 120, 125, 126, 129, 132, 134, 135, 138, 144, (n=14)	133, 159, (n=2)	108, 124, 139, 147 (n=4)

At entry to the study, differences were identified in the report of emotional and psychological problems between men and women. Women reported concern over social rejection and subsequent isolation, the ability to provide financially and emotionally for their children and fear, specifically about their health in the future. Women also worried about their partner's health, particularly partners who didn't take their medication. They were concerned both for the health of the partner and worried about taking care of their partner when he became unwell:

It used to bother me and even now it does, because we feel that if he's taken ill, I'm the one who will suffer in caring for him. ID 119, female, 37 years, intervention

All but one of the men (ID 077, who reported clinically significant benefit) reported that they did not experience any worry or sadness, apart from stress due to the severity and persistence of their physical complaints:

There was a lot of pain on my legs, and indeed this affected my whole body making my situation very miserable. ID 123, male, 44 years, intervention

Their concerns were more about the lack of cure for HIV or their material provisions. They also reported acceptance of their HIV positive status.

My worries were not because of the sickness, I was comfortable that I was positive. ID 156, male, 40 years, control

When queried about why one participant was so calm, he attributed it to trusting in God and in predestination (ID123). It is difficult to extrapolate from these baseline differences whether these differences are between those who reported clinically significant benefit or not, or gender differences.

Results 2: Results by objective

Improvement in mental health and well-being was often hindered by persistent physical symptoms or financial constraints, which were expressed differently across genders. One man described how the anxiety of financial constraint was exacerbated by the lack of understanding displayed by other members of the family, who had expectations of being provided for:

You know when you don't have a job and you are married, you have a family, you have kids, meeting their expenses can sometimes be challenging, and this can also lead to a lot of anxieties within the family, especially when you try to explain to your wife the problems you are facing and she seems not to understand. ID154, male, 32 years, intervention

In terms of self image, women, much more than men, reported a change of perspective during the study period:

Essentially, in that counselling, I was taught how to appreciate myself and never to look down on myself. I was also taught how to live with my children and the family in general, and that those things that look big and scary can be overcome. So the biggest things to me and the most intimidating were anxiety and stigma. So when I was told that all those amounted to nothing and advised to trust in God I suddenly started to see things in a clear perspective. ID 125, female, 30 years, intervention

Women often described some sort of restoration of self, of strength or of a sense of normality, attributed to the education and support they received through participation in the study:

You enlightened me about this condition and the importance of my life. This made me to change and go back to my normal state and be like any other person. ID 106, female 39 years, intervention

I used to be taught that if I get sick...that I shouldn't be troubled in my mind; I should feel normal like any other person and never dwell on the disease... [hesitates] as if I'm suffering in isolation. ID 119, female, 37 years, intervention

Women described a process from feeling worthless and sometimes suicidal, to beginning to accept their situation and their HIV positive status and accepting themselves as a result:

Interviewer: Why do you think you improved?

Participant: Acceptance from within myself

Interviewer: From yourself?

Results 2: Results by objective

Respondent: Yeah, from within myself. Acceptance – this is not the end. Surely, something good will come out of this. Surely I can do better than this. ID 134, female, 41 years, intervention

They began to express compassion for others: considering how others might benefit from hearing about their experience and feeling concern for others who were discouraged and they described spontaneously counselling other HIV positive patients in positive living. Women reported more incidences of stigma and shame than men; situations in which they felt embarrassed about their HIV positive status or avoided situations which would give people in the community cause to talk about them.

I used to tell them that I have my sisters I visit at Bomu who have helped me psychologically and emotionally, though I would tell them that I suffered from T.B. ID 125, female, 30 years, intervention

The fear of and experience of enacted stigma, leading to shame and social isolation, was commonly reported amongst women.

In summary, men reported more benefit in ability to share in quantitative terms, but reported few psychological or problems in the semi structured interviews. It is possible that they were more reluctant to talk socially, outside of the study setting, compared with women, but found that they could share with the researcher, which was what was captured in the quantitative data. The women reported more change in terms of self image, self esteem and positive self identity, which appears not to have been captured by the outcome measures included in this study. This apparent divergence probably reflects the differing aspects of mental health and well-being measured by the differing methodological approaches.

Education

In the quantitative analysis, higher levels of education are associated with worse psychological quality of life and worse ability to share over the study period.

Table 6-17 Distribution of clinically significant benefit across education and study arm in phase 2

	Clinically significant benefit		No clinically significant benefit	
	Control	Intervention	Control	Intervention
Primary school education or less	077, 130, 157, 158, (n=4)	075, 106, 114, 119, 125, 126, 129, 132, 135, 144 (n=10)	097, 133, (n=2)	123, 124, 139, 147, (n=4)
Secondary school or higher	107, 143, (n=2)	110, 120, 134, 138, (n=4)	156, 159, (n=2)	108, 154 (n=2)

Results 2: Results by objective

Amongst those who reported clinically significant benefit, those who had attained secondary school level education or higher reported increased openness as a valuable aspect of their participation. They appreciated the time and attention given to facilitate open exchanges between the study team and participants, and felt empowered to take charge of their healthcare:

Now I feel that there is a way I can deal with myself. I know that if this happens, I can do this and alleviate my pain, alleviate my sufferings and I can take charge – I feel now I can take charge of my life and the things that I do. ID 134, female 41 years, intervention

Those with less education reporting clinically significant benefit spoke more often about the importance of normalisation. The palliative care nurses and the study team treated all participants with a non-judgemental attitude, warmth and acceptance; therefore those who received the intervention were regularly advised to see themselves as normal:

They told me to talk my condition as a normal situation. I shouldn't be shocked. They said I should conduct myself like I used to.... and I should never feel different. So whenever I used to come here, they used to advise me on the same and I said to myself if this is how it is then I should not have any worries aha, so I stopped worrying at all. ID 126, female, 54 years, intervention

Those in the control study arm appreciated the warmth and openness with which they were treated, which made them feel supported and worthy of support:

In fact I liked the way you'd ask me how I was feeling and then I'd explain to you how I was faring. I really felt good – I'd feel the sense of liberation. And that made me cheerful. Because ... [hesitates] you know sometimes you could just be there, in pain, or in distress or something of the sort and you don't even have anyone to ask you, "How are you feeling?" ID 157, female 48 years, control

Participants with less education who did not report improvement reported persistent problematic physical symptoms, lack of social support and financial concerns:

My health condition was ok, but then my only companion who was my mom felt sick, So I got confused because we were both sick and I was helpless. It is at this point that my health started dropping down. ID 97, male, 43 years, control

That was brought about by stress, you know [I] am jobless and when I sit at home, I only think on how to get money and how I will be helping myself, that's where the problem comes from....eeh...lack of job and basic needs in the house, my mind never settled. ID 124, female 37 years, intervention

Results 2: Results by objective

Participants with secondary school education or more who did not report clinically significant benefit reported difficult life circumstances, such as marital discord or more commonly unemployment and financial concerns:

Actually we had a problem with his [her son's] dad.... He just turned to be a drunkard and I didn't want that. He doesn't care about taking care of the kids and what not. So ID 108, female, 37 years, intervention

One of the major issues that I had at that time was financial constraint. I had suddenly lost my job following an unforeseen shakeup at my then workplace. I had no choice but to run here and there looking for a job. ID 154, male, 32 years, intervention

The qualitative data does not clearly appear to explain why those with more education reported worse psychological quality of life and worse ability to share over the study period. In the intervention study arm, those with more education attributed more importance to openness and equal exchange with the staff. Those with less education attributed more importance to the normalisation of HIV.

Wealth

In the quantitative analysis, the wealthiest participants reported improved psychological quality of life and decreased psychiatric morbidity over the study period.

It is important to note that although some participants were relatively better off they were still poor compared with others in Kenyan society, and still experienced financial constraints. Qualitative data were interrogated for patterns comparing these groups, amongst those who reported benefit and those who did not.

Table 6-18 Distribution of clinically significant benefit across wealth and study arm in phase 2

	Clinically significant benefit		No clinically significant benefit	
	Control	Intervention	Control	Intervention
Lower wealth	077, 130, 143, (n=3)	075, 110, 120, 126, 134, 135, 138, 144, (n=8)	097, 159 (n=2)	108, 123, 124, (n=3)
Higher wealth	107, 157, 158, (n=3)	106, 125, 114, 129, 132, 119, (n=6)	133, 156, (n=2)	139, 147, 154 (n=3)

Amongst participants who reported clinically significant benefit, there were few major differences in terms of problems and symptoms between those who were more or less wealthy. Those less wealthy in both the control and intervention study arm more often reported appreciation for the

Results 2: Results by objective

reimbursement for transport, which they used for school fees, food and other necessities. This alleviated financial pressure and enabled them to concentrate on their well-being:

During the times I used to come here and you gave me that [financial] support...I was thinking that now that I have gotten this support, what should I do to improve my health further so I started concentrating in order to get myself from that stress. ID 130, female, 42 years, control

Amongst those with higher levels of affluence, those who reported no clinically significant benefit reported more financial difficulties and appreciation for the transport reimbursement more often than those who reported benefit. They also reported stressors in their social and familial life, such as marital discord or familial rejection due to their HIV diagnosis:

I felt as if now my family had, you know, abandoned me. Then after a while, my mother accepted the truth of the matter... and from that time onwards, any time I have a problem and call her she always chips in. If I need any assistance from my family they also chip in. ID 154, male, 32 years, intervention

Those who were relatively less affluent reported persistent physical complaints, which they perceived prevented them from improving in other areas.

6.3.2.6. Summary of qualitative longitudinal response

The findings from the qualitative data analysis of participant experience and longitudinal response to participation in the study, in terms of mental health and well-being will now be summarised, followed by a discussion of the barriers and facilitators to therapeutic benefit.

Before the study

At baseline many participants reported fear. Fear was health related, associated with ignorance and lack of adequate knowledge about HIV, mistrust of health care professionals and medication and of the social consequences of disclosure of their HIV positive status – potential rejection and discrimination. Participants also reported shame associated with their diagnosis of HIV and the blame they experienced from those in their community, from whom they did not receive acceptance or integration. This social rejection and isolation caused sadness and reduced their social capital expressed through social support which further exacerbated their financial burdens. This also caused significant stress and anxiety. Participants were anxious about their ability to provide, fulfilling their social role both financially and socially for their families, both now and in the future.

Results 2: Results by objective

Persistent physical illness was also cited as a source of anxiety and sadness, causing some to lose hope and express suicidal ideation.

During the study

During the study, those who reported benefit in the intervention arm described how they were empowered by the normalisation of HIV they experienced through their participation in the study. This normalisation positively affected their self esteem, self image and self confidence. They described how important it was that they were treated with acceptance and respect, which alleviated their sadness and anxiety, and improved their self image. They also described how receiving the right medication which addressed their physical complaints eased their psychological concerns that they would not be able to get better. The control group appear to emphasise the associations of physical and psychological problems, describing how the conversations they had with the researcher when completing the outcome measures relieved their emotional burdens, which in turn reportedly relieved the burden of physical complaints.

Those who did not report clinical benefit, in both intervention and control study arms reported intractable physical, social or financial problems, particularly those which meant that they could not fulfil their social roles, which directly or indirectly led to financial difficulties. This in turn led to stress which was a barrier to positive mental health and well-being.

Participants in the intervention arm, even when they did not report clinically significant benefit, described appreciation for the compassionate approach they perceived in the study team. They appreciated being listened to, and the time taken to examine all aspects of their lives in a holistic way. The control patients reported how important it was for them to have a forum to discuss how they lived and how they felt, how the care, attention and social support they perceived from the researcher prompted them to take better care of themselves. They also described how the openness with which they were treated helped them also to be more open, and express themselves more freely.

Longer term effects of participation

After the study, those who reported clinical benefit in the intervention arm reported increased motivation and sense of hope: making plans for the future and considering their legacy. They described the effect of improvement in their physical and social function and their appreciation of being able to fulfil their previous roles. Those in the control arm reported increased self-confidence and ability to talk openly, which increased their opportunity for social interaction and decreased worry through sharing their emotional burdens.

Results 2: Results by objective

Participants in the intervention benefitted from being reassured that they were normal: particularly those who were less well educated. This appears to have been an important component of the intervention: being told that they should see themselves as normal and not sick, and being treated with respect, and not as stigmatised individuals.

Whether they reported clinical benefit or not, all intervention participants described their dissatisfaction with the care they received in the standard care clinic in terms of interactions and opportunity to share emotional burdens. They noticed the lack of therapeutic relationship in this context, which they attributed to a lack of available time to talk. Participants in the control group described how they missed the opportunity to think and talk about their burdens as the study was now over.

Those in the intervention group who did not report clinical benefit described how their holistic well-being had improved and remained positive. Participants in the control arm described how they had continued to feel free as they were instructed during the data collection sessions, and had increased in courage and hope as a result of their participation.

Feeling free was a concept which was often mentioned by both study arms, and was a term used by the researcher when encouraging the participants to respond openly and honestly when completing the patient reported outcome measures. It is possible that this term “freedom” was remembered and reported in the semi structured qualitative data interviews, because it did not appear to be a familiar concept in the lives of the participants.

Model of barriers and facilitators to therapeutic benefit

During analysis of the qualitative data to address this objective, associations emerged between the descriptive phrases participants used to describe well-being, which had been collated into the simple model of the participants understanding of the concept of well-being (Figure 33). These associations highlighted the barriers and facilitators to therapeutic change experienced by the participants during participation in the study.

For example, participants frequently reported that those who were ‘well’ had access to food and could eat well. They described how those who were ‘well’ were able to work or had adequate financial support. Through analysis of the participant experience, it became apparent that these two aspects of wellness were connected; if the family had adequate food to eat, it was seen as an outward sign that the provider of this family was fulfilling their social role, through paid employment or securing other financial support. Eating well was also associated with physical well-being and

Results 2: Results by objective

having the physical capacity to work, and therefore provide for the family. Being unable to fulfil their social role was extremely distressing for many participants, and was associated with worry and sadness:

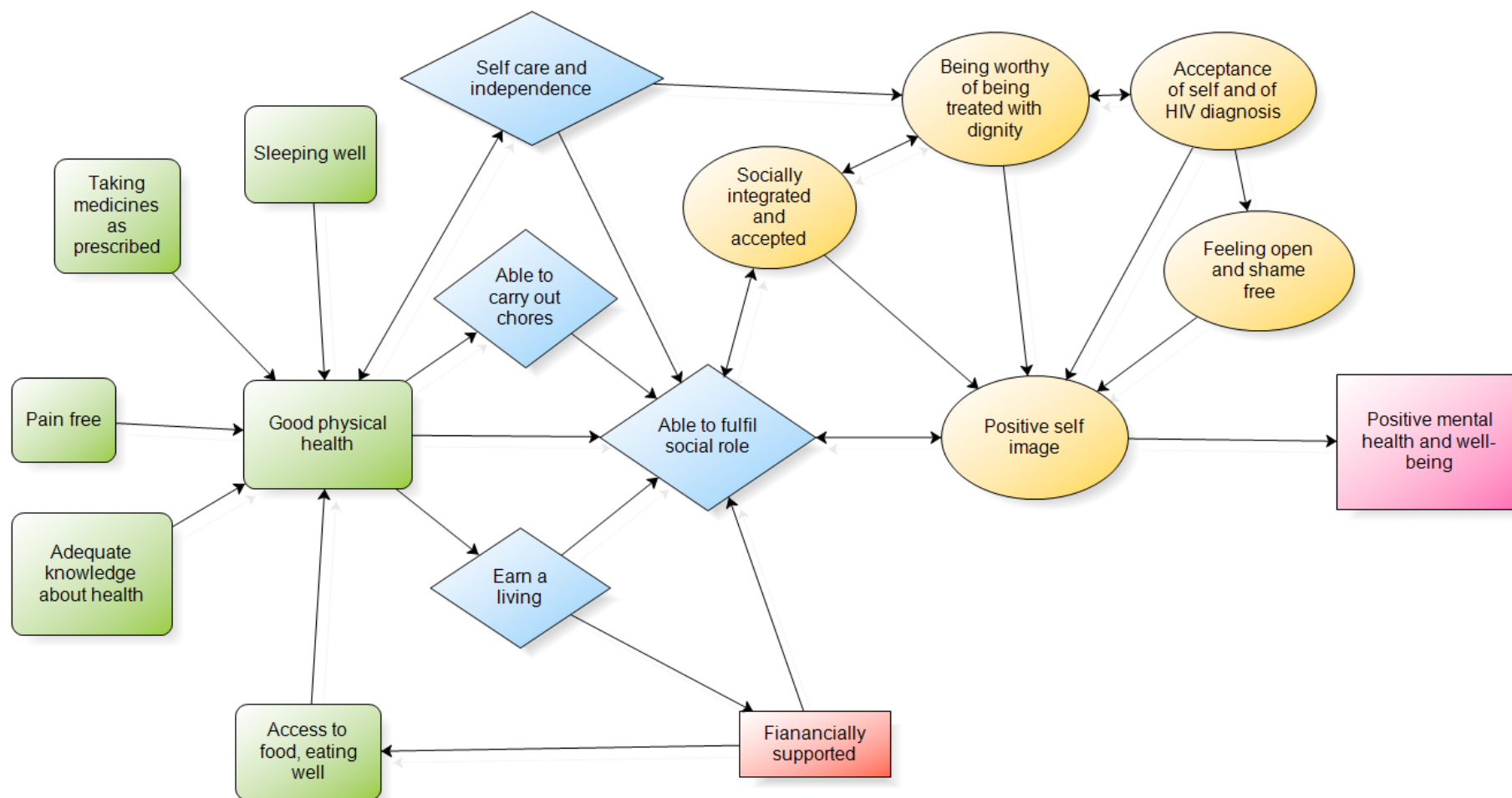
Because, now I was weak, I couldn't work. There was nothing that I could do for myself. I had to depend on somebody to do everything for me. And when they wouldn't do it fast I'd get snappy and I'd get very annoyed you know... Because they were not doing it the way I'd want it done or the way I'd do it. So I'd feel, you see – they are looking down on me. ID 134, female 41 years, intervention

The model was therefore modified to make the identified associations clearer. Descriptive phrases which concerned similar aspects of a concept were combined and associations were inserted into the model using arrows to indicate direction (Figure 34). Through identification of these themes and associations, the model consolidates and presents the facilitators and barriers to therapeutic benefit.

In the model, descriptive phrases relating to physical well-being are presented in green rectangles, social well-being in blue diamonds and socio-relational and individual well-being in yellow circles. Financial support, which intersects with physical and social contributors of well-being, is presented in a red box. This model appears to suggest a process of therapeutic benefit which echoes Maslow's hierarchy of need: physical needs must be met first, which enable the fulfilment of social role which contributes to positive self image and mental health and well-being (364).

Results 2: Results by objective

Figure 34 Facilitators and barriers of mental health and well-being during participants experience of the study



Poor physical health was described as a barrier to positive mental health and well-being. This was explained by fears of future ill health and the implications this might have on the participant's ability to fulfil their social role, whether that was care taking in the home or earning a living in paid employment. Fulfilment of social role was also associated with feeling socially integrated and accepted, and also to positive self image. Positive self image was associated with feeling open and shame free, accepting oneself and one's HIV positive diagnosis and being treated with and feeling worthy of dignity and respect.

6.3.3. Summary of quantitative and qualitative findings

Improvement in mental health and well-being during the study period was dependent on the resolution of physical, social or financial concerns regardless of participant study arm. Those who had overcome these reported improved mental health and well-being.

Those whose physical problems were not addressed continued to suffer, reporting fear that they would not improve, and concern regarding their lack of understanding of why they continued to experience pain and symptoms. Those who experienced social problems such as gender-based violence or rejection from their families continued to experience poor mental health and well-being. Those who benefitted from couples counselling during receipt of the intervention, or who challenged the stigma and discrimination they were subject to, experienced improved mental health and well-being. Those who experienced continued financial constraint continued to experience poor mental health and well-being.

Men reported fewer mental health concerns on recruitment; and appeared to be more comfortable with their HIV positive status. This confirms the quantitative finding, that women had more psychological and social problems at baseline. Quantitative data identifying increased ability to share over time in men compared with women was not explicitly explained by the qualitative data.

Participants with more education appreciated the openness with which the study team interacted with the participants, whilst those with less education reported more appreciation from being reassured that they were normal, regardless of their HIV positive diagnosis.

All participants reported experiencing financial constraint.

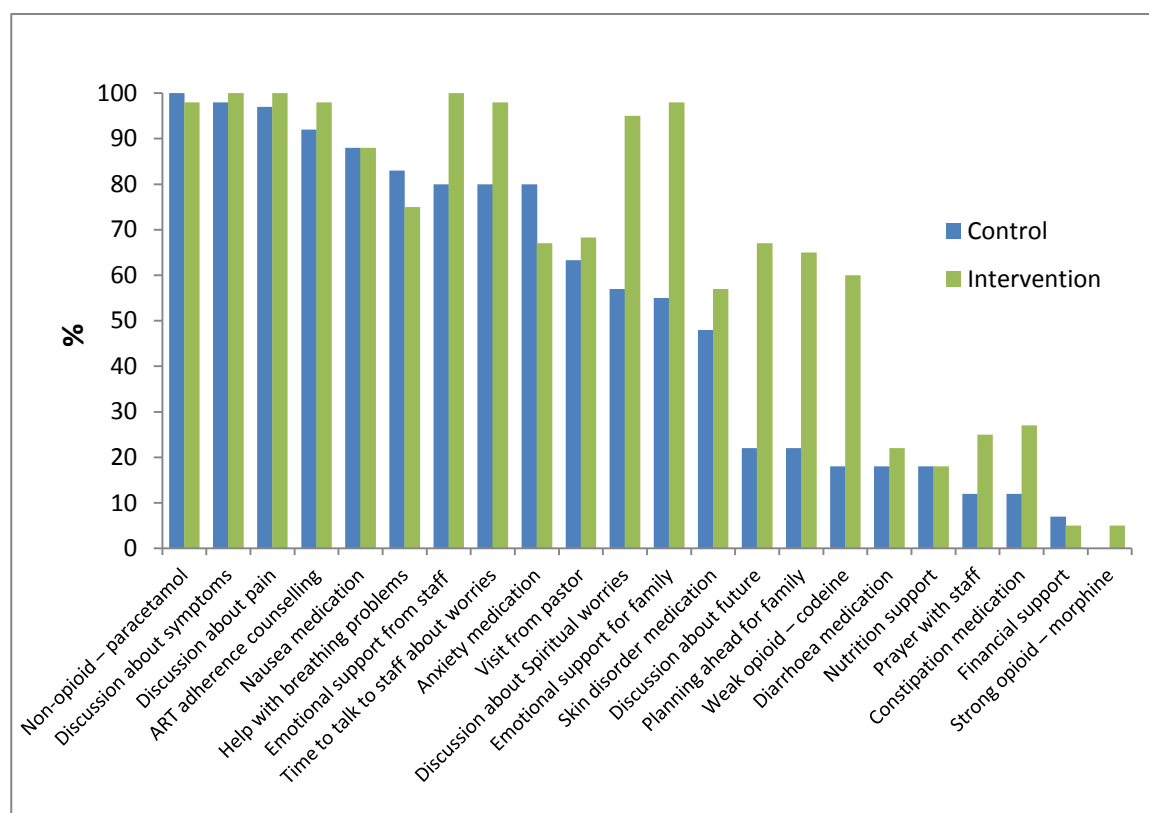
6.4. Objective 4

To identify and explore the existence of “active ingredients” and mechanisms of action of the intervention and therapeutic aspects and processes of study participation.

6.4.1. Components of palliative care delivered as part of the intervention

A comparison of service receipt data by control and intervention study arms is depicted in a bar chart (Figure 35).

Figure 35 Bar chart of participants who ever received components of care, by study arm



This graph shows that those in the intervention arm appeared to have received more emotional support from staff, time to talk to staff about worries, visits from their pastor or imam, discussion about spiritual worries, emotional support for their families, skin disorder medication, discussion about the future, planning ahead for family, weak opioids, prayer with staff and constipation medication. All variables were analysed to identify statistically significant differences between service receipt in control and intervention participant groups (Table 6-19).

Results 2: Results by objective

Table 6-19 Summary of number and percentage of participants who ever received components of care, by study arm

Service	Control % (n)	Intervention % (n)	χ^2 test and p value
Visit from spiritual leader	63.3 (38)	68.3 (41)	$\chi^2=0.33$ p=0.56
Discussion about spiritual worries	57 (34)	95 (57)	$\chi^2=24.1$ p<0.001
Prayer with staff	12 (7)	25 (15)	$\chi^2=3.56$ p=0.06
Emotional support from staff	80 (49)	100 (60)	Fisher's exact p<0.01
ART adherence counselling	92 (55)	98 (59)	Fisher's exact p=0.21
Time to talk to staff about worries	80 (48)	98 (59)	Fisher's exact p<0.01
Emotional support for family	55 (33)	98 (59)	Fisher's exact p<0.01
Discussion about pain	97 (58)	100 (60)	Fisher's exact p=0.50
Discussion about symptoms	98 (59)	100 (60)	Fisher's exact p=1.00
Non-opioid – paracetamol	100 (60)	98 (59)	Fisher's exact p=1.00
Weak opioid – codeine	18 (11)	60 (36)	$\chi^2=21.9$ p<0.01
Strong opioid – morphine	0 (0)	5 (3)	Fisher's exact p=0.24
Help with breathing problems	83 (50)	75 (45)	$\chi^2=1.26$ p=0.26
Anxiety medication	80 (48)	67 (40)	$\chi^2=2.72$ p=0.10
Nausea medication	88 (53)	88 (53)	$\chi^2=0.00$ p=1.00
Skin disorder medication	48 (29)	57 (34)	$\chi^2=0.84$ p=0.36
Diarrhoea medication	18 (11)	22 (13)	$\chi^2=0.21$ p=0.65
Constipation medication	12 (7)	27 (16)	$\chi^2=4.36$ p=0.04
Discussion about future	22 (13)	67 (40)	$\chi^2=24.6$ p<0.01
Planning ahead for family	22 (13)	65 (39)	$\chi^2=22.9$ p<0.01
Nutrition support	18 (30)	18 (30)	$\chi^2=0.00$ p=1.00
Financial support	7 (4)	5 (3)	Fisher's exact p=1.00

Statistically significant differences are evident between control and intervention study arm in discussion about spiritual worries, emotional support from staff, time to talk to staff about worries, emotional support for family, receipt of weak opioids, discussion about the future and support for the family in planning for the future. All differences benefit the intervention arm. Other than receipt of weak opioids, all variables indicate that the intervention group received more social, spiritual and emotional support.

6.4.2. Active ingredients

Active ingredients were identified through analysis of data from phases 1 and 2, the results of which are reported consecutively below.

6.4.2.1. Phase 1 Quantitative data analysis to identify active ingredients

Statistically significant associations between components of care and mental health and well-being in intervention arm participants are shown in Table 6-20. As presented in Figure 35 and Table 6-19, almost all intervention group participants reported receiving emotional support from staff, ART adherence counselling, time to talk to staff about worries, emotional support for family, discussion with staff about pain and discussion about physical symptoms. Due to this co-linearity, analysis of these variables was not possible.

All of the participants who received discussion about spiritual worries, non-opioid analgesia, strong opioid analgesia and anti-emetics during the study period reported either high or low AUC for as a whole group, and therefore this analysis was unable to produce a valid odds ratio due to insufficient variation. This is indicated with a ‘-’ in the table. This analysis indicate that all participants who received discussions about their spiritual worries reported high levels of psychological quality of life, low levels of psychiatric morbidity and low levels of ability to share feelings. All participants who received paracetamol reported high levels of psychological quality of life, low levels of psychiatric morbidity and worry, but low ability to share feelings. All participants who received morphine reported low levels of psychological quality of life, high levels of psychiatric morbidity and low ability to share feelings. All participants who received anti-emetics reported high levels of psychological quality of life.

The analysis also found a statistically significant association between a visit from a spiritual leader or receipt of codeine and increased odds of improved ability to share feelings with friends and family over the study period.

Results 2: Results by objective

Table 6-20 Logistic regression for effect of receipt of each component of palliative care using AUC data

Component of care	Odds ratio, (95% confidence interval) and p value (n=54)			
	MHSS AUC	GHQ AUC	APOS worry AUC	APOS share AUC
Visit from spiritual leader	1.38 (0.31-6.14) 0.67	0.76 (0.19-3.11) 0.71	1.22 (0.33-4.50) 0.77	5.39 (1.38-21.05) 0.02
Discussion about spiritual worries	-	-	1.31 (0.09-18.53) 0.84	-
Prayer with staff	1.14 (0.26-4.98) 0.86	1.02 (0.22-4.68) 0.98	0.75 (0.16-3.45) 0.71	2.45 (0.65-9.20) 0.18
Non-opioid (paracetamol)	-	-	-	-
Weak opioid – codeine	1.13 (0.25-5.17) 0.87	1.96 (0.46-8.30) 0.36	1.24 (0.36-4.29) 0.73	4.46 (1.35-14.76) 0.01
Strong opioid – morphine	-	-	4.44 (0.29-67.12) 0.28	-
Help with breathing problems	1.09 (0.23-5.10) 0.92	0.51 (0.10-2.53) 0.41	0.72 (0.18-2.89) 0.64	0.33 (0.09-1.22) 0.10
Medication to help with worrying or feeling sad	0.94 (0.23-3.87) 0.93	1.64 (0.40-6.72) 0.49	1.67 (0.49-5.71) 0.41	1.39 (0.43-4.56) 0.58
Medication for feeling sick	-	2.26 (0.18-28.88) 0.53	3.33 (0.34-32.29) 0.30	2.51 (0.37-17.09) 0.35
Medication for skin problems	0.32 (0.08-1.27) 0.11	1.07 (0.27-4.23) 0.93	1.91 (0.58-6.32) 0.29	2.22 (0.71-7.00) 0.17
Medication for diarrhoea	0.90 (0.20-4.13) 0.89	0.57 (0.12-2.85) 0.50	1.30 (0.33-5.08) 0.71	2.53 (0.59-10.87) 0.21
Medication for constipation	1.37 (0.29-6.38) 0.69	0.43 (0.09-2.01) 0.28	1.19 (0.32-4.40) 0.79	0.91 (0.26-3.18) 0.88
Discussion about future	1.43 (0.33-6.16) 0.63	1.51 (0.35-6.59) 0.58	1.10 (0.31-3.86) 0.88	3.15 (0.92-10.79) 0.07
Planning ahead for family	0.63 (0.13-2.95) 0.56	2.82 (0.58-13.93) 0.20	1.72 (0.48-6.25) 0.41	1.33 (0.39-4.53) 0.65
Nutritional support	2.67 (0.61-11.66) 0.19	1.66 (0.39-7.16) 0.50	1.06 (0.28-4.01) 0.93	3.26 (0.86-12.34) 0.08
Financial support	0.91 (0.05-15.36) 0.95	1.02 (0.08-13.35) 0.99	1.06 (0.08-14.64) 0.96	0.23 (0.02-2.87) 0.25

The finding that a visit from a spiritual leader increases the odds of participant reporting high ability to share over the study period, whilst discussion about spiritual worries was associated with decreased ability to share is surprising and difficult to explain. It would be expected that discussions with a spiritual leader would be about spiritual concerns and therefore the outcomes of the discussions would be the same regardless of where they were held. It is possible that this is a chance finding.

The other finding from this analysis which is interesting is the association between poor mental health and well-being and receipt of morphine. Further examination of the data revealed that there were five prescriptions for morphine administered during the study period to three patients, one of whom was terminally ill and died before study exit. It is important to also recall that this analysis is cross sectional and therefore no direction of causality can be suggested.

6.4.2.2. Phase 2 Qualitative data analysis identifying the active ingredients of the intervention

Three active ingredients were identified in the qualitative data: insight and understanding, taking time to talk, and medication. These are discussed in turn with their associated mechanism of action.

Insight and understanding

The concept of insight and understanding was the most often cited active ingredient and was a major theme in the data with two sub themes: health education and counselling. These sub-themes were often difficult to disentangle, as the terms appeared to be used interchangeably by some participants.

Effective counselling was mostly concerned with what the study nurses termed “prevention with positive living”. This is a component of the Kenyan care programme for PLWH, and encompasses advice on how to live with a diagnosis of HIV in a positive way. Prevention with positive living also included basic guidance on reducing sexual transmission of the virus and how to interact with the community and with family regarding disclosure and management of discrimination:

What benefited me most was the guidance on how to live positively, commitment to church and being prayerful. That I should always pray when faced with difficulty, eat well and will have a long life. ID 132, female, 45 years, intervention

Together with the study nurses, the participants were able to identify and address substantial unmet health education needs during the delivery of the intervention:

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They counselled me and told me that it was important to observe my health status, especially on proper feeding. They also talked to me about sexuality and about my family.... It kept on improving because there were many things that I had not known about that the nurses taught me. ID 120, female, 36 years, intervention

The nurses helped me; yes, my needs were met because my needs included the need for advice; the importance of taking my medication. ID 75, female, 42 years, intervention

I was wondering what to do because she would insist, "Try to eat as much as possible, whatever is available. You don't have to force yourself but little by little, make sure you don't go hungry". So I purposed to be keen on feeding well especially on food items known for boosting the blood in the body such as fruits – I fully devoted myself to the practice and by the time I was coming back the next time, everything was going up, up. ID 125, female, 30 years, intervention

Having this information enabled the participants to make informed decisions regarding their healthcare:

Initially, I didn't take medicine at the right time. But when I came here, they told me that I needed to take medicines at the right time because that would help me. Then I ought to eat well, do some exercises, read the Bible and I'd live longer. ID 110, female, 28 years, intervention

Finally, participants described how, increased information increased their capacity to manage their own condition, and increased their belief in their own ability to cope:

The questions that you [researcher] used to ask me have improved my physical well-being in such a way that when I come here, let's say I talk to the other [study] nurse, we discuss more about the HIV epidemic. I may be asked questions such as what leads to a person being infected and how to prevent. We'd also talk about the moral support I used to receive from you people.... I have made me feel as if, though internally I know I'm HIV positive but on the other side I feel as if I'm no longer sick. I'm just like any other person out there who is not HIV positive because whenever I come here, I get my medicines. And I know if I take them as required I might have some more years to live. ID 154, male, 32 years, intervention

Mechanism of action: adequate information

Having adequate information through increased insight and understanding empowered the participants to take their medications as prescribed and make decisions which would benefit their health. It also reduced negative psychological symptoms such as sadness and fear, arising from a lack of knowledge of what they might face in the future.

Results 2: Results by objective

Respondent: I was no longer anxious

Interviewer: What freed you from anxiety?

The advice that you gave me when I came here, such as about this disease – whether it would last or not last.... whether the disease is for life or not. ID 119, female, 37 years, intervention

But after coming here, the advice that you gave me really supported me. I started thinking positively about my life and believed that I could have a long life. ID 110, female, 28 years, intervention

Having access to the information they need to look after themselves, was associated with alleviation of depression and fear:

I was in depressive moods but later, owing to the constant guidance you gave to me and my realization of the worthiness thereof, I started getting committed in my mind and adhering to your instructions. ID 106, female, 39 years, intervention

Yes I used to cry... it used to seem like the end of the world to me [laughing]... But I came here and got good advice from you...ID 129, female, 43 years, intervention

Counselling is available also in standard care, and it is interesting to consider why the provision of information was effective in palliative care but not in standard care. I will return to this point in section 7.3.2.1.

Medication

Long standing symptoms such as numbness or pain resolved during receipt of appropriate medication through the intervention care package. Relief of physical pain and distress contributed to an overall reduction of holistic distress, and a return to previous levels of physical and social function:

Whenever you found me to be sick, you got me the required medication free of charge. That helped me and kept me going for a long time and I started appreciating myself again, you see what I mean? From that time my problems eased and from around half a month to a month and a half, I started to feel like I had resurrected. I felt like I'd come out of the grave. ID125, female, 30 years, intervention

It is not clear whether the medications prescribed as part of the intervention care package were previously unavailable or inappropriately prescribed by the standard care clinic. It could also be hypothesised that health education meant that medications were better understood and regimens therefore better adhered to:

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I was distressed but I came here and was put under medication, got better and went on well with my work. Right now I have no problem at all and I feel that my life is much better. I was helped with guidance, counselling and on the importance of sticking to medication ... and I got healed. ID 132, female, 45 years, intervention

Mechanism of action: symptom relief

Being pain- and symptom-free and experiencing physical health, meant participants could increasingly care for themselves and were able to earn a living and provide for their dependants, which alleviated stress and contributed towards their positive self-image. Participants reported that access to non opioid and mild opioid analgesia was associated with improvements in mental health and well-being:

If I came for treatment, say today, for a new case, I think after giving me the medicines I'd be relieved the following day.... Yes, I'd be relieved. It didn't persist. ID 119, female, 37 years, intervention

The pain eased because of the drugs that I took – the ones that I was given. They cleared off the numbness and once that was over the exhaustion also gave way... But since I recovered from that numbness, I can now move around, I can go to work and I can do anything. ID 123, male, 44 years, intervention

Restoration of physical health also contributed to the process of normalising HIV infection, which improved mental health and well-being:

To me, that was the most important thing because when I came here, my legs got well again and I started working, I felt like a normal human being. ID 123, male, 44 years, intervention

Taking time to talk

The third active ingredient was taking time to talk. The increased time to talk to the study nurses, helped the participants to articulate their needs, which meant that the advice they were given was more personalised, more often addressed the root cause of the symptom, and was therefore more therapeutic:

I think I am better because I was listened to; I was helped. I was given advice and so I left with something. ID 108, female, 37 years, intervention

The additional time the study nurses were able to spend time with the intervention participants compared favourably with the experience in the CCC, where increased patient numbers unavoidably means reduced patient-staff contact time:

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When I go there [CCC], we don't have time to talk even though they are the same people I'm used to meeting every time. We don't have time to share, but when I come to this side, we talk, share and if I have any problem I raise it up. ID 154, male, 32 years, intervention

Here, we have more time with them; they will not see you in a hurry like the other place [CCC] because there are other people waiting; here you will be seen; you will explain your problem. ID 108, female, 37 years, intervention

Time spent with the study nurses was structured according to the assessment sheets designed to be used as a guide to holistic assessment. It is also possible that the time spent with the study nurses was therapeutic, because this time was structured according to this assessment.

Mechanism of action: articulated concerns

The mechanism of action of this active ingredient was that participants concerns were more clearly articulated, which enabled the study nurses to gain a greater understanding of the problems and increased the chance of them being addressed:

There is a difference because here you have a lot of time to be with the doctor, to talk to him/her and to have them instruct you. But on the other side, not that the nurses are unwilling, but you personally feel condemned and say, "Ah there are others who are waiting to come in". So you may be having issues that you'd want addressed but you feel, "Ah, I'll raise when I come next time". But here you feel free to ask anything without any problem. ID 120, female, 36 years, intervention

As a result of being properly listened to, the nurses' advice and the treatment prescribed was more personalised, appropriate and more effective:

When you go to the ordinary clinics there is no time a sister will sit down with you and tell you this and this.....they only give you drugs or push you in to see the doctor, but when you come here you have to talk first, you have to discuss You see it's good when you come here because even if you have other ailment, the advice they will give you will make you feel much better. ID 124, female, 37 years, intervention

Their interactions with staff were therefore more fruitful, and addressed educational needs in a more targeted way, which affected physical and mental health and well-being.

6.4.2.3. Summary of active ingredients

Findings from analysis of the CSRI data from phase 1 showed that participants in the intervention study arm received more emotional support for themselves and their family, time to talk about their

worries (including the spiritual) discussions about the future and support for planning for their family in the future. They also received more weak opioids (codeine) than those allocated to the control arm. Further analysis identified statistically significant positive associations between the receipt of paracetamol, codeine and anti-emetics on components of mental health and well-being and a negative association with receipt of morphine.

Discussions of spiritual worries appeared to be positively associated with psychological quality of life and negatively associated with psychiatric morbidity (both indicating improvement in well-being). Surprisingly, the association between discussion of spiritual worries and ability to share was identified as significant and negative, whereas a visit from a spiritual leader was significant and positive.

Analysis of phase 2 qualitative data identified three active ingredients and the mechanism of their action. These were increasing insight and understanding, which addressed unmet health information needs, medications, which relieved physical symptoms and taking time to talk, which helped participants articulate their concerns, enabling the nurses to tailor responses more appropriately to address participant problems.

These mixed method findings converge with strong evidence to suggest that medications such as analgesia (paracetamol and codeine) and anti-emetics are associated with benefit in terms of mental health and well-being. Table 6-19 shows that whilst almost all participants received paracetamol, more participants in the intervention arm received codeine. This suggests that stronger analgesia is necessary in the medical management of these patients, and effective pain management has a beneficial effect on mental health and well-being.

All but one intervention participant received all psychosocial components of care, including time for discussion and provision of emotional and social support, although their effect on the outcome measures was not able to be analysed in the quantitative data analysis. Time to talk and insight and understanding were found to be associated with benefit in the qualitative findings, suggesting that health education and counselling and time to talk are important active ingredients of the intervention.

In summary, the active ingredients of the intervention identified through analysis of quantitative and qualitative data are effective medication, including analgesia, the provision of effective health education and counselling and increased taking time to talk:

Nobody had the time and chance to talk to me about how to take my drugs in a better way. So when I came here, you guys – what can I say? You counselled me and you taught me how to use my drugs in a better way. ID 138, female, 40 years, intervention

6.4.3. Therapeutic aspects of participation

Analysis of the data from phase 2 of the study showed that participants in both intervention and controls groups reported benefit from participation in the study.

These five themes which emerged during the analysis of qualitative data are described as therapeutic aspects of participation: compassionate care, the therapeutic benefits of talking, social support, patient reported outcome measures (PROMs) as prompts and material support. They were often expressed slightly differently by participants allocated to receive either the standard care or intervention care package, therefore the similarities and differences between participants accounts' from each study arm will be identified and discussed in the narrative report which follows along with their associated therapeutic process.

6.4.3.1. Compassionate care, social support and communication

These three therapeutic aspects of study participation were found, on closer examination, to be associated with the same therapeutic process, i.e. they exert their therapeutic power in a similar way, through trusting relationship. For this reason, they will be reported consecutively in one section followed by a description of the action of the therapeutic process of trusting relationship.

Compassionate care

Compassionate care encompasses two sub themes: feeling treated well and being known. The perception of the study team as compassionate appeared to be grounded in the non-judgemental attitude of the team members, which participants interpreted as openness and supportiveness. This is well articulated by a woman allocated to the intervention arm:

Interviewer: Why do you think this happened, like why were you able to open up?

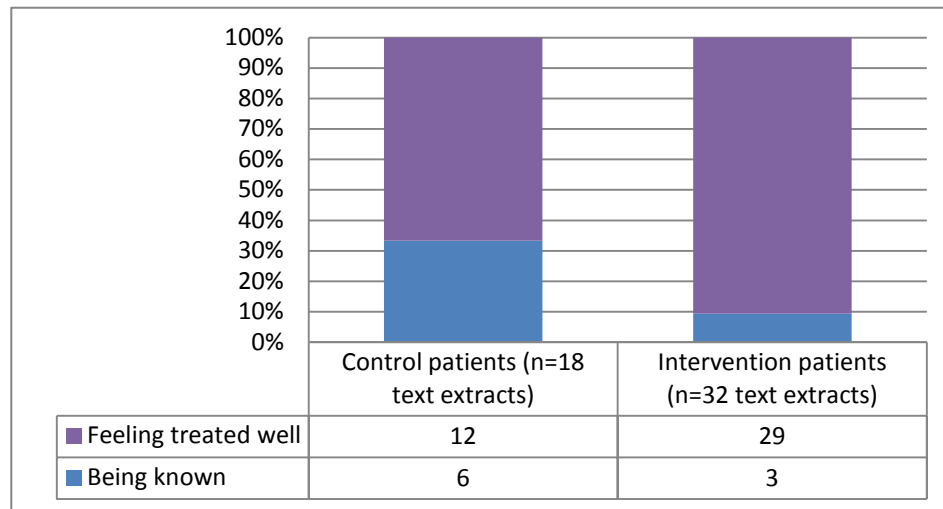
Respondent: The attention I received, the care, I mean, I would say the attention that I first received and the care. ID 134, female, 41 years, intervention,

The graphic representation of the distribution of text extracts coded at the two sub-themes presented in Figure 36 shows differences in the way intervention and control participants experienced compassionate care. It is important to note in the interpretation of this percentage stacked bar chart, and the ones which follow, that this is the total percentage of text extract coded

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at a theme, and does not represent all participants included in the sample. The chart is provided to indicate the relative importance of each sub-theme for participants, by study arm.

Figure 36 Distribution of text extracts for sub-themes of compassionate care, by study arm



Feeling treated well

As shown in Figure 36 the most frequently reported aspect of compassionate care was appreciation of being treated well, which was described as being treated and spoken to in a caring, friendly, warm and respectful way:

I used to be soothed such as being treated well, I mean I felt esteemed, that people here regarded me and treated me with respect. ID 106, female, 39 years, intervention

You'd feel that they were really caring. They were concerned, they were happy to see you – it's not like you were a bother. It was not like it was something too big – like you were bringing in problems; no it was about helping one another. You see (hesitates) ... I would look forward to, "Tomorrow I'm going to the clinic, yes, yes ..." ID 134, female, 41 years, intervention

The way you treat people, talking to people nicely and knowing how they are proceeding health wise, so many things that make one feel better already. ID 129, female, 43 years, intervention

This view was also expressed by participants in the control:

Another thing is the way you handle patients. For instance one may come here broken hearted and feeling down but you would encourage and give him the best, so many things contributed to this change. ID 158, female, 33 years, control

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So when I came here I feel it really helped me because I found ... [hesitates] that day, I found people who were very free and they talked to me very nicely. The way I was received – I really appreciate. ID 107, female, 46 years, control

Intervention arm participants described the welcome they received from the study nurses as important to their well-being:

Personal touch, the way they would welcome me, the way they would welcome you and you'd feel at home you know. You'd feel that they were really caring. They were concerned, they were happy to see you – it's not like you were a bother. ID 134, female, 41 years, intervention

The care they received increased their sense of being at ease and that they were not a problem which was therapeutic:

You know, whenever I came here I would feel at peace, you know. Not like some places you'd go and feel unsettled. Here you'd come and feel at home. ID 138, female, 40 years, intervention

Being known

The perceived interest that the study team took in the health of the participants was noted, particularly by those allocated to the control arm. They appreciated having someone check on their progress, and take an interest in their problems:

There's one thing that I have liked about this research, and that is when you would want to know about the progress of my health. That motivated me and made me to feel good. ID 157, female 48 years, control

The most important thing is the way you were concerned with my life and daily activities, you used to ask if I have attended the clinic and so forth. And again the fact that the TOPcare study team is interested in knowing our progress as the patients is important to me as well. ID 158, female, 33 years control

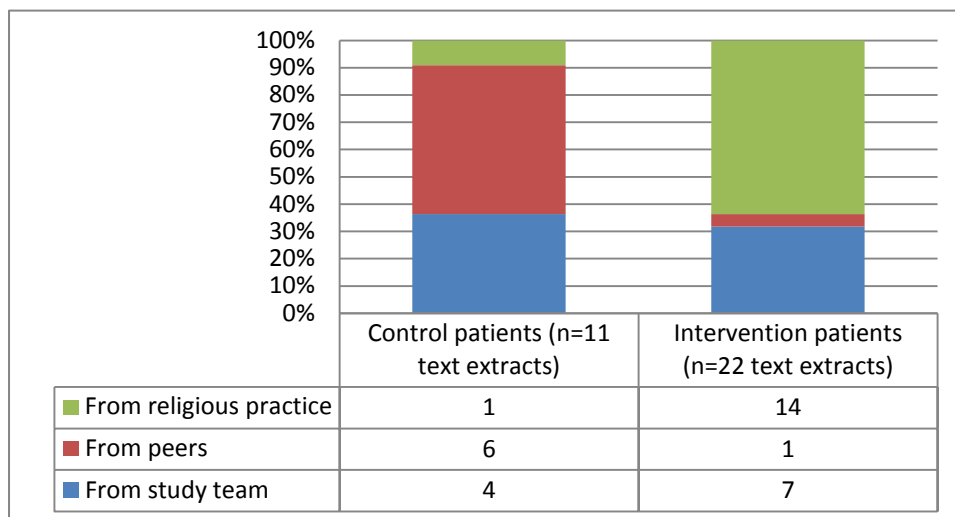
Compassionate care helped the intervention participants concentrate on expressing themselves, without fear of recrimination or negative reaction.

Social support

Social support was described as a therapeutic aspect of participation, with sub-themes of support from religious practice, peers and study team.

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Figure 37 Distribution of text extracts for sub-themes of social support, by study arm



From religious practice

The importance of support from religious practice was described much more frequently by the intervention arm participants (cited by one control arm participant). They described the connectivity and social engagement of religious practice as very helpful. The study nurses encouraged the participants to engage in religious practice as part of the intervention, encouraging the participants to seek support from pastors or imams, attending public services if possible and read scriptures and pray in private:

You know the other sister used to share the scriptures with me - from the book. Yes, the Bible, as she read the word, those many thoughts I used to have would vanish from my mind....The pain also eased... Yes, I got relieved. ID 144, male, 32 years, intervention

Some participants reported attending services and feeling benefit from the social connectedness to their church family, or reading the Bible or praying and feeling connected to the Divine. This connection was a source of comfort and of strength:

[Now] I go to church always. It has helped me because whenever I go to church I feel happy and peaceful. ID 126, female, 54 years, intervention

From peers

Befriending peers as a result of participation in the study was important for many participants, but more frequently for those in the control group. They began to see that there were many people who had experienced similar things to them, from the diagnosis and medical care to stigma and discrimination. As a result of increasing courage which she attributed to participation in the study,

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one participant described how she had disclosed her HIV positive status, which led to the discovery that she had peers.

What actually happened, from the day that I disclosed my status to my family and my friends, from that time, things started working for me – because they began supporting me, they began to be close to me and I found that we were the same and we were all sailing on the same boat. ID 143, female, 36 years, control

Participants reported increasing strength from the knowledge that there were many people in the same situation, whether they had made contact with them or not.

The more I used to come here for questioning the more I got encouraged, to get that advice that I should not worry, as I am not alone in this sickness. We are many despite the fact that we don't know each other encouraged me the more. ID 97, male, 43 years, control

From the study team

Participants in the intervention study arm described the study team (researcher and two nurses) as friends from whom they received social support which they described as therapeutic:

It was more personal and attached. I mean you would feel that there was a link... The nurse was feeling for you, she was relating to what you were going through. She was concerned, there was some concern. You would feel that there was someone who was there to help you to mourn with you. You see, you were not all alone. ID 134, female, 41, intervention

They also described the palliative care nurses as 'buddies' or 'helping hands', from whom, even after study exit, they anticipated a supportive friendly response. One participant from the intervention study arm reported how she returned to the palliative care nurses for comfort after study exit when she felt frightened about the anticipation of a pap smear test.

The sense of care which the participants perceived from the study team was important for participants in both study arms. They described how they developed feelings of friendship between themselves and the study team and grew to enjoy their company:

They have changed me a lot because as I came here frequently, I became social to those people who used to interview me and I wish I would continue with the sessions and even if not so, then I would love to have some talks with them about life. ID 159, female, 30 years, control

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Yeah you don't take us as if – these are sick people, you know. You treat me like a fellow human being, like your sister, like your ... you know, friend – genuine friend. That's more important. ID 138, female, 40 years, intervention

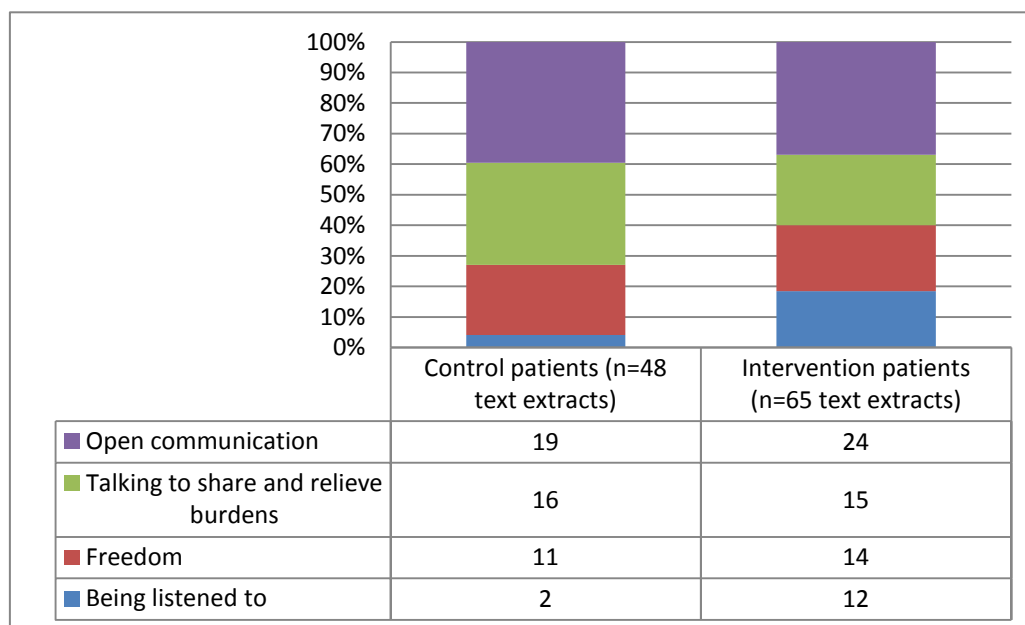
Interactions with the study team and, for those in the intervention group, with the study nurses was described as supportive by many participants, and contrasted with their experiences interacting with staff in the CCC:

There was a link, there was a bond, there was something – I mean that feeling that she's with you. There was feeling. The nurse was feeling for you, she was relating to what you were going through....You would feel that there was someone who was there to help you to mourn with you. You see, you were not all alone. So, but unlike at the C.C.C., you see you are many and it's like, "This is your medication go over there and take". ID 134, female 41 years, intervention

Communication

The theme of the communication contained four sub-themes: open communication, talking to share and relieve burdens, freedom in communication and being listened to.

Figure 38 Distribution of text extracts for sub themes of communication, by study arm



Open communication

For participants, openness was an essential aspect of communication, both in terms of the way questions were asked and the way participants felt when they were answering them. Essentially, participants perceived the researcher's accepting attitude as communicating her personal acceptance, which was a powerful experience for many participants who were socially isolated or

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who had experienced stigma or discrimination. The acceptance and openness which was built between the researcher, study nurses and the participants facilitated the disclosure of previously un-discussed topics:

The way I'm talking to you now there are things that I cannot talk with other doctors or other sisters out there. Here I'm free. ID 138, female, 40 years, intervention

Communication provided space for the participants to organise their thoughts and the opportunity to explore their current situation and reflect on how they would like to respond to their current situation, an opportunity they may otherwise not have had:

When I used to come here, we would talk with you and you would ask me the questions and I'd reflect back... So I would think about it – reflect, reflect about it... and once I'd reflected, I'd sit down over and think now, something should change. ID 134, female, 41 years, intervention

The open communication during data collection appointments was also appreciated by participants, who described how the open way in which the questions were asked encouraged them to express themselves, which made them feel liberated:

Coming here has really helped me, especially for that freedom and I feel liberated.... Yes it has helped me to express myself. ID 107, female, 46 years, control

Every time that we talked, I'd have relief from pain. Because the questions you used to ask were about things affecting me psychologically. So whenever you asked a question and after I'd provide the answer - that problem would get out of my life. ID 110, female, 28 years, intervention

Sharing burdens for relief

Participants often described the psychological relief felt after sharing a problem:

I also shared my problems as they occurred - you know, you don't solve problems by keeping them to yourself but by sharing with other people. That way, you feel a bit of relief. ID 154, male, 32 years, intervention

You know when you are being asked such questions, you feel like your mind is being set free. So I used to feel like ... basically, say, as I was leaving here, I felt as if something ... [hesitates] that also contributed in improving my psychological well being. It really helped it to improve. ID 120, female, 36 years, intervention

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Participants allocated to the control study arm, who were only completing the outcome measures during data collection appointments and not receiving counselling, also reported benefit from communication:

When I started coming here, the worries started going down because I found somebody whom I could tell my problems and when I started doing that then the depression started going down. ID 143, female 36 years, control

You helped by asking me several questions on what was affecting, I felt like someone was helping me to carry my burden, I had problems with solving my issues but whenever I came here and you advised me all was ok, and I found it simple to solve them. ID 130, female, 42 years, control

Feeling free

The safe and welcoming therapeutic environment enabled intervention arm participants to express themselves freely and openly:

I was scared because I have never had an opportunity like this to explain myself and I have never been questioned like this before, but as times went by, I started talking freely and stopped being scared and I was much happy because you told me a lot of things in a free manner...so I became much free to you unlike at the beginning of the study. ID 135, female, 50 years, intervention

The sisters were so good to me and I loved them just as they loved me. And this gave me a lot of freedom. So there was a difference – here I had more freedom than the other place. ID 125, female, 30 years, intervention

The study team encouraged participants to express themselves freely and interacted with them in a way which was perceived as free and open by the participants:

It also helped me because when I started going there I used to be afraid but after coming here and got to be asked the questions, I started answering expressly, I found it to be of much help because I started feeling free... The type of questions that I was being asked and the way I was being asked, freely it also made me to feel free... ID 107, female, 46 years, control

Participants were treated with respect and were asked to decide which language they wanted to conduct the appointment in. This made self expression easier for some:

It was easy because first of all, one would use a language of their [own] choice. You didn't have to use the language preferred by the nurse. Then you'd feel the sense of freedom. It was

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easy because it would be between you and the doctor alone. It was private. ID 120, female, 36 years, intervention

Beyond the content of the discussions, participants described benefit from verbally expressing their concerns:

Every time that we talked, I'd have relief from pain. Because the questions you used to ask were about things affecting me psychologically. So whenever you asked a question and after I'd provide the answer - that problem would get out of my life. Yeah. ID 110, female, 28 years, intervention

Being listened to

Participants also described their appreciation of having somebody take time to listen to them:

Psychologically, you know you need somebody who you can share your problems with, at least he's your buddy, him or her, and you feel settled down. ID 138, female, 40 years intervention

For intervention arm participants, being listened to was akin to taking time to talk, described as an active ingredient of the intervention missing in standard care:

It was never meaningful [in the CCC] because when you get here you have to talk and discuss is when you proceed to treatment... and there, is all about presenting your card to the doctor and you receive drugs that's all. ID 124, female, 37 years, intervention

Mechanism of action: trusting relationship

Without trust, participants cannot begin the vulnerable task of rebuilding a sense of positive self-image. Trust is defined in the literature as the mutual understanding that no party will exploit another's vulnerability and is recognised as essential to human well-being (365). Trust is formed between individuals on the basis of social interaction, where one expects the other to act in a non harmful way, without established contractual obligation (366). .

Many participants in the study were subject to stigma and discrimination on a daily basis (see page 171), which undermined their sense that they were worthy of time and attention, of friendship and of being treated with dignity and respect, which contributed to a negative self image. This was compounded by the lack of time available for the nurses in the CCC to show their interest and to adequately discuss participants' problems. Having a trusting relationship counteracts the effect of stigmatising messages received by the participants from their immediate and wider communities, which were damaging to their positive self image, mental health and well-being. The therapeutic

Results 2: Results by objective

process described by the participants is a shift from seeing themselves negatively, through internalisation of stigmatising messages, to seeing themselves as normal – just like anyone else.

Compassionate care

Compassionate care and its two sub-themes (feeling treated well and being known) communicated to participants that they were worthy of being treated with dignity and respect in the context of a trusting relationship, which contributed to positive self image.

Based on how we started, the way you showed me the importance, you enlightened me about this condition and the importance of my life. This made me to change and go back to my normal state and be like any other person. ID 106, female, 39 years, intervention

I started viewing myself like any other person, as you see me now, like am not sick at all I stopped worrying about myself and focused. ID 129, female, 43 years, intervention

As previously described, being encouraged to treat themselves and see themselves as normal, and worthy of being treated with respect within a trusting relationship, despite the diagnosis of HIV was extremely important for many participants. This effect was more marked in the intervention participants, who were repeatedly told that they were normal by the palliative care nurses. Participants' emphasis on the benefits of being told that they were normal suggests participants experienced feelings of abnormality. Similarly, the extent to which participants repeatedly reported appreciation for the compassion and care from the study team suggests that this was not in abundance in other areas of their lives. This lack of feeling normal and compassion from others contributed to participants' feelings of negative self-image, fuelled by the experience of stigma and discrimination.

Social support

Receiving social support and forming trusting relationships communicated to the participants that they were worthy of trust, social integration and acceptance, which contributed to a positive self image:

It helped me because when we used to discuss I felt we were more close. ID 124, female 37 years, intervention

As described in the findings from objective 3 (page 148) many participants experienced social rejection or feared that they would experience rejection if they disclosed their status:

Results 2: Results by objective

I used to feel all alone because I struggled with everything on my own, I used to feel that telling anybody my problem wouldn't help instead they would only laugh at me and isolate me the more. ID 129, female, 43 years, intervention

Strong, trusting relationships built with the study team and subsequently with their peers and with others through religious practice, improved self image, and enabled them to access their previously un-accessed agency:

It's true because even now, at the moment, I can stand in front of people and open up but before I came here I couldn't do that..... The way I used to come here and you'd speak to me made me realize that there was no need of keeping things to myself anymore. I resolved to speak out so that I could be helped in whichever way.... When I started coming here, the worries started going down because I found somebody whom I could tell my problems and when I started doing that then the depression started going down. ID 143, female, 33 years, control

This increased trust, social acceptance and support appeared to offer a counter-narrative to the social rejection participants feared they would meet in the community. Social stigma in the form of discrimination was described as a normative aspect of culture and, when internalised, had evident damaging effects on the participant's positive self image:

I felt guilty and responsible for my sickness so I felt like even if I cry to God he will never listen to me. ID 139, female, 42 years, intervention

I never use to view myself as normal and at times I used to ask myself what I would do to be like others because I had no meal, I had stress, drugs are required and I had no money. ID 130, female, 42 years, control

Participants reported isolating themselves from potential sources of support, particularly when describing their experiences before recruitment to the study, and living in fear of the reaction of their friends and family if they discovered the HIV positive diagnosis:

What if my relatives got to know about my status before I had disclosed it? What about my beautiful daughter, how she would react? Such things. Those were my worries. ID 143, female, 33 years, control

The rebuilding of self image occurred through the experience of developing trusting relationships, and participants began to reject the stigmatising messages that they were abnormal, inferior or had reason to be shamed and keep their diagnosis secret:

Results 2: Results by objective

I was scared when I first started this study, and my health was also not in a good condition when I started but as I came here for the discussions I started feeling ok, because I became free and started living my life as normal and when I told my family about my health, they also joined hands in supporting me. ID 135, female 50 years, intervention

The most important thing to me was the fact that I realized how to stay contented with this disease, not to be afraid or despise myself but to look upon everything as usual and trust in God. ID 097, male, 43 years, control

It is because when you used to ask me questions, I used to feel much free inside ... I felt like a very normal person without any form of illness, I felt so good eh. ID 126, female, 54 years, intervention

Through rebuilding self image and sense of worth, by means of positive, trusting, supportive relationships and social interaction, the participants were able to overcome their fear and engage with those in their community.

I think [people engage socially now] because I am a happy person right now and I pay them visits as well, I also feel that they see me living a normal and doing my own work without fear. Unlike before, I never used to talk to anyone even if they would pay me a visit and that bored them from coming but everything is normal right now. ID 158, female 33 years, control

Communication

Aside from the content of the interactions, which are captured elsewhere (section 6.4.2.2), the findings of this analysis show that in receiving compassionate care and social support, control and intervention group participants were able to build a trusting relationship in which they were able to verbally express themselves in a therapeutic way. Communication also exerted its therapeutic power because of trust.

The combination of trust, adequate time and the confidentiality of the study team interactions with participants created a unique environment for the participants to discuss their problems freely and openly. Because of the stigma of HIV and the associated secrecy, participants described finding it difficult to find a safe forum in which to discuss their concerns, or plans for self-care:

Because if you seek advice from anyone – you ask them, “Is it okay for me to do this”, they’ll start talking ill about you everywhere. ID 107, female 46 years, control

Participants felt safe to express themselves openly, without fear of judgement, which enabled them to process their experiences and emotions, and begin to accept their situation without shame:

Results 2: Results by objective

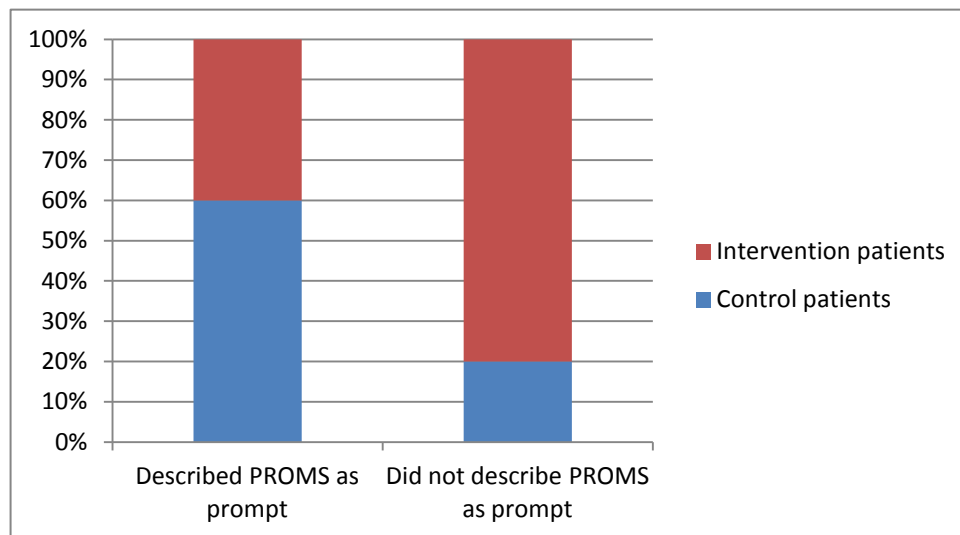
The most important thing was ... most important thing of being here was being able to express myself. To accept what has become of me and to say that this is what is happening but I can overcome it. This has been very nice and then a forum of expressing my innermost feelings and fears. ID 134, female, 41 years intervention

But after being spoken to every so often, I went over it and accepted that it was only a condition that would come to pass and that I'd go back to my normal life. ID 106, female, 39 years, intervention

6.4.3.2. PROMs as prompts

While both control and intervention participants reported using PROMs as a prompt to reflection, identification of problems and self care, this was especially common in the control arm participants possibly because they did not receive any other explicit input. Figure 39 presents the number of participants in each arm who reported using the PROMs as prompts, to illustrate these differences.

Figure 39 Distribution of participants referring to PROMS as prompts, by study arm



The questions, asked at each data collection appointment were described as a mind exercise, without which improvement would have been slower:

Sitting down to be asked questions made me better, because were it not for those questions it would have taken me a lot of time to get back to my normal psychological status. So asking those questions acted like exercising my mind. ID 120, female, 36 years, intervention

That someone was interested in the extent of support they received, or the frequency with which they attended the clinic or took their medication, was taken as an indication of the importance of these components of self care:

Results 2: Results by objective

I told you that I sometimes I would forget. You asked me “why” and since you asked that question “Why” ... I went back home and adhered to the prescription and I have never skipped taking medicine apart from the day I had an operation. ID 107, female, 46 years, control

Once the pain was off and ... when I used to come here, we would talk with you and you would ask me the questions and I’d reflect back. You know, I would go over my ... I’d reflect back, whatever that you had asked. So I would think about it – reflect, reflect about it ... ID 134, female, 41 years, intervention,

Others described adhering more closely to their prescribed ART or other health promotion messages so that they could report positive news to the researcher at the next appointment, with a clear conscience. Some control arm participants perceived therapeutic benefit from completing the PROMS, similar to the experience of receiving counselling:

There are some questions amongst the questions that you used to ask me, that I have never been asked by anyone before in life, not even with my family member. There are some questions that my family members have never asked me since I contracted this disease and those questions that you asked me made to learn that there is life even after being positive. ID 159, female, 30 years, control

In terms of health education, many control arm participants had gaps in their knowledge – about HIV, healthy eating and nutrition, family planning and protected sex and the importance of adhering to ART. Some described how the PROMS helped them think, and increased their suspicions that there was something they should have been doing which they were currently not.

They could ask me every time if I was using a condom, so I suspected there was a mess in not using a condom so I decided to use it. ID 156, male, 40 years, control

This also highlights the lack of basic knowledge in the patients attending the standard care clinic.

Therapeutic process: self care

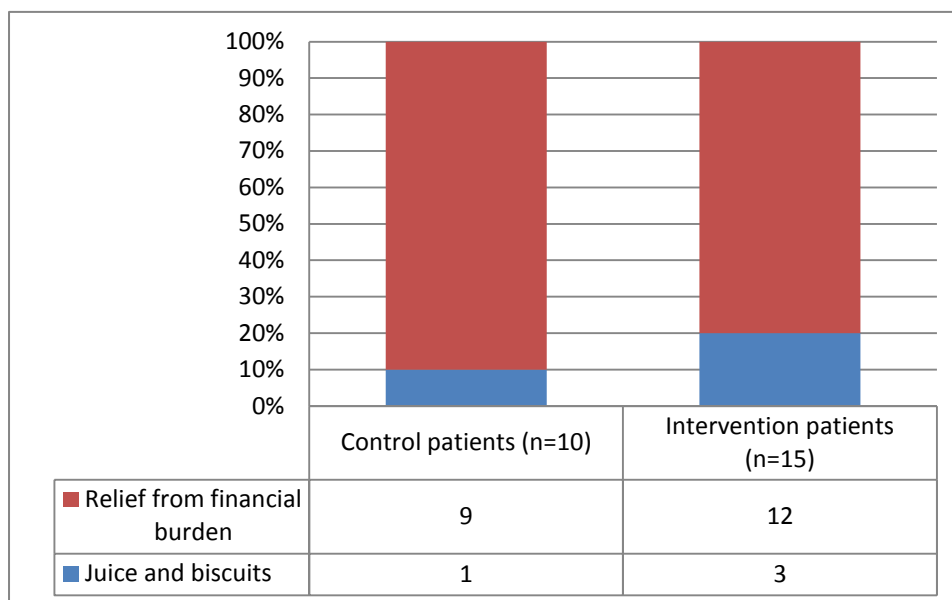
Participants reported using the PROMS to prompt self-care, as a trigger for health promotion, self care and a structure for self reflection, which continued once they left the data collection appointment.

To be honest when I first came here and sat down with you for a discussion I felt different... the discussion we used to have made me feel at peace and I got rid of all the bad thoughts I had, on my way home ... so I started helping myself to change step by step. ID 130, female, 42 years, control

6.4.3.3. Material support

All participants in the trial were supported materially in two ways: light refreshments on arrival at the research centre, and reimbursement for travel expenses (US\$5).

Figure 40 Distribution of text extracts for sub-themes of material support, by study arm



Participants in both arms reported appreciation for the refreshments. For some this was seen as an extension of the hospitality of the research visit, as a sign of dignity, respect, affirmation or support:

Interviewer: What did they do for you to feel treated well or soothed?

Respondent: First and foremost when I came here I'd be appeased with biscuits and juice....then I would be given the fare and then I'd be given good medicines. ID 106, female, 39 years, intervention

In Kenyan culture, receiving guests with light refreshments is seen as basic hospitality and not to do so in social situations would be an insult to the guest. It is possible that this gesture of hospitality and understanding of social norms, laid the foundations for the development of the therapeutically beneficial relationships with the study team that participants described.

The reimbursement for travel expenses was often used by participants to support other expenses, such as to purchase a higher quality of food or to provide for some of the needs of their families. Some reported using the money to pay school fees or to contribute towards costs of a wedding:

As it was, I couldn't go on with my work at that time because I wasn't in good health. So after getting that transport money, I would use it for transport and then I'd have some to buy

Results 2: Results by objective

some food items. So that helped a great deal and that's why I was continually motivated. ID 120, female, 36 years, intervention

I stopped being worried, feeding well, as well as helping me financially to buy the food so that I could feed well. ID 114, female, 48 years, intervention

I will go there and they'll reimburse my fare – that fare I'll use it ... something else that's small that may be I was lacking – I can buy ... maybe I can buy even some fruits and what have you on my way home. So I'd feel, "Huh, there is something. There is something to look forward to. ID 134, female, 41 years, intervention

The control participants also reported using the travel reimbursement to buy tonics or medications they might otherwise not have been able to access. This relieved the financial burden they were under to some extent, and was cited by many as a source of therapeutic benefit:

I'd get prescription from there and sometimes if I came here I'd be given something like bus fare. That bus fare would really help me, using it for fare and I'd use like a 100 shillings on the prescription. I can say that I used to benefit. ID 107, female, 46 years, control

The transport reimbursement alleviated this financial burden which was a source of stress and therefore a barrier to positive mental health and well-being in both study arms. This was also evident in the data from a participant in the intervention group who reported clinically significant deterioration, which she attributed to persistent financial pressures, that she could not see a way of alleviating.

Therapeutic process: relief of financial strain

Financial strain was a source of concern for many participants therefore this small alleviation of the constraint was cited by many as a reason for their reduction in anxiety. In addition to relieving financial constraint, this financial support enabled participants to be more self determining, increasing their ability to access items which were important to them which were otherwise unavailable.

This improved the ability of participants in both study arms to fulfil their social role in provision for their family, and in turn improved their self image as a provider, or contributing member of the social group. Fulfilling this role in a way which was socially expected contributed towards improvements in self image and positive mental health and well-being.

6.4.4. Summary of active ingredients and therapeutic aspects of participation

The mechanism of action of the identified active ingredients and therapeutic processes of the aspects of participation identified in the analysis of qualitative data, are mapped onto the model created to address objective 3, illustrating the barriers and facilitators to therapeutic benefit (Figure 34). The actions of the active ingredients and therapeutic processes are mapped using coloured bars to highlight the processes affected.

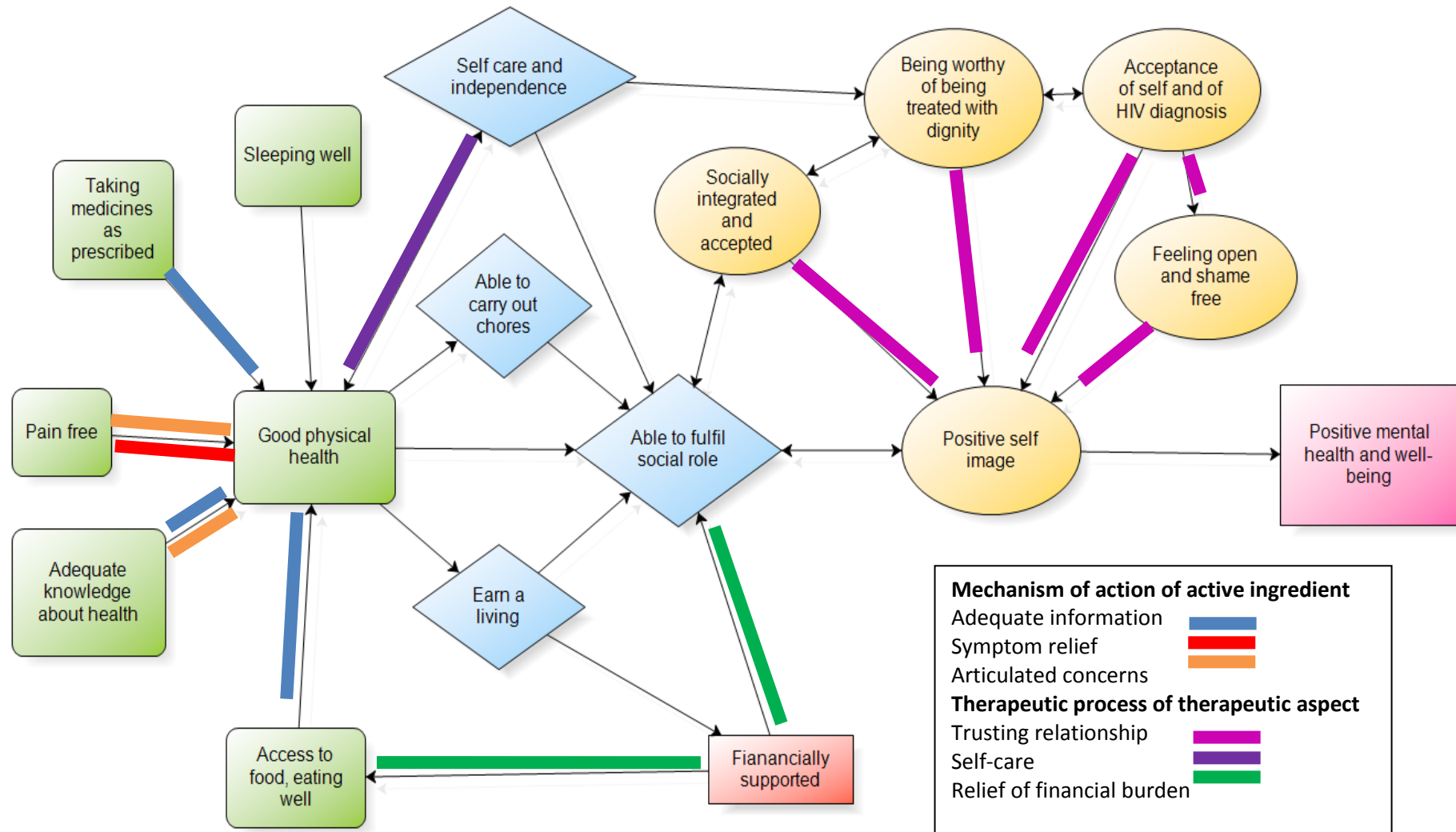
The mechanism of action of the active ingredients appears to improve physical well-being, by management of symptoms through provision of effective medication, improving health promoting behaviours through education and counselling and addressing the problems of patients through providing time to articulate symptoms and concerns. This improvement in physical well-being enables the participants to fulfil their social role.

The process of the therapeutic aspects of participation appears to have had effects on social role and self image. Building trusting relationships increased participants' feelings of social acceptance and integration, acceptance of self and decreases their feelings of shame and the need to isolate themselves. The trusting relationships also gave the participants an experience of being treated with dignity and respect. This enhanced participant self image which led to improved mental health and well-being. Self-care through use of PROMs as prompts increased physical well-being and increases independence. And the provision of material support enables participants in both study arms to fulfil their social role and expectations and increased self determination, in that they could chose how the money was spent, which contributed to physical and mental health and well-being.

Having good physical health and fulfilling one's social role promotes positive self image and positive mental health and well-being in this sample.

Results 2: Results by objective

Figure 41 Mechanism of action of active ingredients and therapeutic processes of therapeutic aspects of participation



6.4.5. Summary of findings from objective 4

Active ingredients of the intervention care package received by those allocated to the intervention study arm (identified through quantitative and qualitative data analysis) were insight and understanding (which encompasses counselling and health education), medication, and taking time. Insight and understanding relieved anxiety and depression associated with ignorance about HIV and about the future which would be possible if participants adhered to their ART. It also enabled participants to make better decisions about their self care; for example, improving their diet. Medication relieved physical symptoms, which were a great sources of anxiety for many participants who were recruited on the basis of moderate to severe pain or other symptoms. Taking time for discussion during the palliative care appointments enabled the intervention group participants to articulate their symptoms and concerns and therefore receive a more targeted and appropriate treatment response.

Therapeutic aspects of participation in the study, experienced by participants in both study arms, were compassionate care, communication, social support, PROMs as prompts and material support. Compassionate care, social support and the communication exerted their therapeutic process were through trusting relationship, which enabled participants to rebuild their self image which had been damaged, in part by stigma and discrimination. The PROMs provided a structure for participants to reflect on their well-being and were used to trigger self care behaviours and highlight health promoting behaviours they should adopt. Material support increased the participants' ability to provide for their families and relieved anxiety caused by financial constraint.

6.5. Summary of all findings by objective

6.5.1. Objective 1

To determine baseline levels of mental well-being and to examine associations between baseline mental well-being and demographic and clinical characteristics among patients with HIV on ART enrolled in a randomised controlled trial (RCT) of a nurse-led palliative care intervention

At baseline, psychological quality of life as measured by the MOS-HIV MHSS, was found to be worse than in the reference population (44.8 compared with 50 (307)), and worse in female participants compared to men ($p=0.02$).

The median score for psychiatric morbidity is approximately the threshold for “caseness”, indicating that half of the sample had some level of psychiatric morbidity at baseline.

Baseline analysis showed that 45% of the sample was worried all of the time and 35% were not able to share their feelings with friends or family at any time in the past 3 days.

There were no associations between psychiatric morbidity, worry or ability to share feelings and age, gender, partner status, number of children, number of financial dependents, highest educational attainment, CD4 count at baseline, receipt of TB treatment, previous AIDS diagnosis or wealth.

6.5.2. Objective 2

To identify any effect of the palliative care intervention on mental health and well-being, comparing the intervention with standard best practice.

Monthly time point analysis identified early statistically significant difference between control and intervention group in all outcomes ($p \leq 0.02$). These differences attenuated for psychological quality of life, psychiatric morbidity and worry, with no significant difference between control and intervention groups by trial exit. The difference in ability to share feelings also narrowed into insignificance at month in ability to share, but then widened at the final time point to reach statistical significance again.

Analysis of repeated measures, adjusting for data correlated by participant identified a positive effect of the intervention on psychological quality of life, psychiatric morbidity and the ability to share feelings, but not worry.

6.5.3. Objective 3

To determine and describe participant experience and longitudinal response to participation in the study in terms of mental health and well-being, and to identify and explore associations between participant response and demographic and clinical characteristics.

Analysis for association between are under the curve for mental health and wellbeing outcomes and clinical and demographic variables found a positive association with wealth and mental health and well-being in terms of psychological quality of life and a negative association with psychiatric morbidity. Increased educational attainment was associated with decreasing psychological quality of life and ability to share feelings. Male gender was associated with increasing ability to share feelings. Allocation to the intervention group was associated with improved psychological quality of life, ability to share and improved psychiatric morbidity. The strongest and most consistent predictor of outcome in each dimension of mental health and well-being was baseline score.

Analysis of qualitative data found that barriers to receiving benefit in terms of mental health and well-being from the intervention were unaddressed physical, social or financial problems. Physical problems were pain and other symptoms and social problems were rejection or gender based violence. Participants described building their self image through participation in the study, and increasingly rejecting the HIV associated stigma they encountered.

6.5.4. Objective 4

To identify and explore the existence of “active ingredients” and mechanisms of action of the intervention and therapeutic aspects and processes of study participation.

Active ingredients of the intervention, identified through integration of findings from quantitative and qualitative data analysis, were insight and understanding, medication and taking time to talk, particularly about psychosocial issues.

Therapeutic aspects of study participation were identified as compassionate care, the therapeutic benefit of talking, social support, PROMs as prompts and material support. The processes through which these therapeutic aspects exerted their power were through increases in trusting relationships and through using the PROMs as a structure for self-reflection and education, thus improving physical health and alleviating strain on mental health and well-being. Material support relieved the anxieties caused by financial constraint.

7. Discussion

This section will summarise the main findings from the quantitative and qualitative analyses by objective, and then discuss and situate the active ingredients and therapeutic aspects of participation within the relevant literature. Limitations of the study and the findings will then be discussed, in addition to ethical implications and future work, in terms of both clinical and academic practice.

7.1. Main findings

This study, for the first time, describes the considerable psychological burden experience by PLWH on ART, with moderate pain or symptoms. It has found that a nurse-led palliative care intervention benefitted participants through health education and counselling, medication and providing time to talk, particularly in the context of a socially stigmatising condition. The study also found that aspects of participating in the study were therapeutically beneficial for participants in both study arms: being treated with compassion, social support, communication, using the PROMs as prompts to self-care and receiving material support.

Barriers to improving mental health and well-being were unmet physical, financial and social needs. This echoes the seminal theory of Maslow, where physiological need (air, food, water) must be realised before higher needs for safety (employment, family resources), love and belonging (friendship, family, sexual intimacy), esteem (self respect and respect of others) and self actualisation can be recognised and addressed (364).

In this chapter, these key findings will be discussed and considered more fully, with reference to the wider evidence and in the context of the aim of the study, restated in Table 7-1.

Table 7-1 Study Aim

<p>To evaluate the effectiveness of a nurse-led palliative care intervention on the mental well-being of HIV patients on ART in Kenya, and to explore active ingredients of the intervention and their mechanism of action and therapeutic aspects of participation</p>

7.2. Effectiveness of a nurse-led intervention on mental health and well-being of HIV patients on ART in Kenya

We found evidence that the intervention was effective in terms of the quantitative measures of psychological quality of life, psychiatric morbidity, worry and the ability to share. These findings are now discussed with reference to the wider literature.

7.2.1. Psychological quality of life

At baseline, the median score for psychological quality of life, as measured by MHSS, was lower than the reference median in the literature (50), indicating worse psychological quality of life (307). Comparison with findings from research in other HIV positive populations indicates that this figure is similar (Table 7-2), despite our sample being recruited on the basis of moderate to severe pain or other symptoms.

Table 7-2 Comparison of MHSS in this study with other study sample

Source	Country	Year	MOS-HIV MHSS (possible range 1-100)
Study sample	Kenya	2012	44.2 (7.7) (median and IQR)
He <i>et al</i> (367)	China	2012	43.6 mean (sd 9.7)
Stangl <i>et al</i> (368)	Uganda	2011	40.0 mean (sd 11.2)
Chariyalertsak <i>et al</i> (369)	Thailand	2010	53.4 (mean)
Ion <i>et al</i> (370)	Canada	2011	49.2 mean (sd 10.7)
DeGroote <i>et al</i> (371)	Belgium	2013	52.0 median (IQR 44.2–57.9)

Women were found to have worse baseline psychological quality of life compared with men. This finding has been replicated in other studies of PLWH in Canada (370), Cuba (372) and Uganda (373). This also mirrors data for the general population, where women are found to have increased rates of anxiety and mood disorders, (although men have higher rates of externalising and substance use disorders) (142, 374, 375). These gender differences have been partially attributed to gender inequality, as a narrowing of difference has been reported where women have increased role equality (374).

In comparison with those receiving standard care, participants allocated to receive the intervention care package reported significantly improved psychological quality of life one month after baseline (T1 of 5 time points) and significant difference was also found at month 3 ($p=0.04$) and month 4 ($p=0.06$) with benefit in the intervention arm. Longitudinal multi level analysis of repeated measures

found a statistically significant difference between control and intervention group participants with benefit in the intervention arm. Thus the null hypothesis of no effect of the intervention was rejected.

Analysis of MHSS AUC (longitudinal summary) showed some evidence of an association between higher psychological quality of life and decreased educational attainment ($p=0.089$). Contrastingly, a study from Italy found that increasing education was associated with improvement in MHSS in an observational cohort of PLWH on ART (376), a finding also reported in two separate studies from Uganda (373, 377), and the USA (301). The results from the analysis of the qualitative data suggest that those with less education reported appreciation from being reassured that they were ‘normal’ more frequently than those who had attained higher levels of education. This could explain this counterintuitive finding.

A positive association between wealth and psychological quality of life was identified in analysis of AUC data in this study. This finding is replicated in other research with PLWH in Uganda (373), USA (378) and Zimbabwe (379). In the general population low socioeconomic status is also associated with poorer outcomes in terms of anxiety and mood disorders (375). This suggests that low socioeconomic status could be a barrier to benefiting from this intervention.

7.2.2. Psychiatric morbidity

The median baseline GHQ-12 score was 6 points, when analysed using the scoring system for those with chronic conditions. As previously discussed, because four different versions of the GHQ questionnaire and three different approaches to scoring the data are evident in the academic literature, there are few comparisons available for the data from this study.

Table 7-3 Comparison of GHQ-12 score in this study with other samples

Sample	Country	Year	GHQ-12 score (possible range 1-12)
This study sample	Kenya	2012	6 median (3-9)
Mixed population with chronic symptoms (380)	Italy	1993	7.46 mean (sd 3.02)
Community sample (311)	UK	1988	8.6 mean

It appears that our score of a median of 6 (data was not normally distributed) is lower than other samples, indicating a comparatively low level of psychiatric morbidity (Table 7-3).

Monthly time point analysis found initial significant difference between control and intervention groups at months 1 and 2 ($p=0.02$ for both), with benefit to the intervention group, which was not apparent at later time points. Longitudinal multilevel analysis of repeated measures found a significant difference between study arms for GHQ-12 score ($p=0.035$) with benefit in the intervention group.

Analysis of association with clinical and demographic variables showed that GHQ-12 was positively associated with poverty ($p=0.04$) suggesting that higher levels of economic deprivation are associated with increasing GHQ-12 score, and by implication high levels of psychiatric morbidity. This is similar to the findings for psychological quality of life, and is in line with the wider evidence that morbidity is associated with poverty and socioeconomic difficulty (375).

7.2.3. Worry

Baseline levels of worry as measured by the APOS indicated that one half of participants were worried all the time (54/120) and one third were not worried at all (34/120).

The APOS is a relatively new measure and thus there is little published data with which to compare this score. A cross sectional study of PEPFAR funded clinic patients in South Africa and Uganda reported a median score of 2 for worry, compared with 2.5 from this study (222).

Monthly time point analysis showed a significant difference in worry at month 1 ($p=0.01$) but at no other time point. Longitudinal analysis of repeated measures indicated no difference between control and intervention group. There were no association between any clinical or demographic variables and AUC analysis for worry.

Nurse-led palliative care has been found to decrease worry or anxiety in patients with advanced cancer (381). The distribution at baseline, (with more than 70% at either end of the scale) suggests that there may have been some difficulties experienced by the sample in interpreting and responding accurately to this question.

7.2.4. Ability to share feelings

At baseline 53% of participants reported that they were able to share their feelings with friends or family at all times in the past three days. The median of 5 reported in this study (0=worst, 5=best) suggests that this sample were considerably more able to share their feelings at baseline than the sample from South Africa and Uganda cited above, who reported a median score of 3 (222).

Monthly time point analysis found statistically significant benefit in the intervention group at month 1 and the final time point of month 4. Longitudinal analysis of repeated measures found statistically significant difference between control and intervention arms for the ability to share feelings, with benefit in the intervention group.

AUC analysis for association of ability to share over the study period with clinical and demographic variables found benefit in men compared with women, and a negative association with educational attainment.

Whilst the APOS item of ability to share feelings does not describe availability of social support, it is a measure of utilisation of social and emotional support. It is possible that at baseline, when no difference between men and women was noted, men were not sharing their feelings, but perceived that their level of sharing was adequate. The qualitative data analysis found that men reported no worries or concerns, which could indicate a reluctance to talk about feelings or that they were accurately describing their state of mind. During the study, as indicated in data from phase 1 and 2, they began to share their feelings and reported increased disclosure of their HIV status and increases in social and emotional support.

A large cross sectional study of the general population in Norway found that increasing receipt of emotional support is associated with lower prevalence of depression, an effect which was stronger in women compared with men (382). A general population based cross-sectional study in Beirut, Lebanon identified a similar trend, where social support was protective of self-rated health for women but not for men (383). This suggests that social support in the form of sharing feelings may not have been important for men in our study before recruitment, but once the study commenced, they began to share with the study team. This does not necessarily indicate that this was beneficial for their mental health and well-being, as evidenced by the lack of effect seen on psychological quality of life and psychiatric morbidity in this study.

There is little published data exploring the association between education level and social support. A cross sectional study from Nigeria found that PLWH who had poor social support also had low levels of education and poor quality of life (103). Cross sectional data from women living with HIV in the USA found that increased social support was associated with social capital variables including educational level (384). However, this evidence does not explain why those with increased educational attainment reported worse ability to share feelings over the study period, and therefore this finding warrants further investigation.

7.3. Sources of benefit: Active ingredients and therapeutic aspects of participation

Active ingredients were identified by intervention participants as therapeutically beneficial aspects of the intervention care package, through analysis of the quantitative and qualitative data, and will be discussed in the context of the wider evidence. Therapeutic aspects of participation, common to both study arms will be discussed subsequently.

Attention to the causal mechanisms of the active ingredients and therapeutic aspects of participation was primed by the critical realist approach taken in this thesis, (described in section 3.3.2.2, Pg 66), which draws attention to the importance of underlying mechanism which drive observable changes. Each causal mechanism and process discovered through data analysis is described after a discussion of the corresponding active ingredient or therapeutic aspect of participation.

7.3.1. Active ingredients of the intervention and their mechanism of action

7.3.1.1. Insight and understanding and adequate information

The theme of insight and understanding encompassed two sub-themes, health education and counselling, which were described by participants as an important source of therapeutic benefit, both in terms of content and delivery.

The need for health information found in the baseline quantitative data was met by health education and counselling delivered as part of the intervention care package. This alleviated participants' fears associated with uncertainty and their future, due to living with HIV.

In the literature, there is pre-existing evidence for the effectiveness of psycho-educational interventions in the reduction of depression and anxiety in mental health and cancer research (226, 232, 233). In palliative care research, cancer patients who received advanced care planning, which includes discussion with patients about the future, were found to have decreased depression (238) and anxiety (237). Findings from the HIV literature that group educational and psychological support are effective in decreasing anxiety, depression and perceived stress, has led to the widespread use of peer support groups for PLWH (230). There is overlap between the active ingredient of insight and understanding and the therapeutic process of trust. Evidence suggests that when delivered in the context of little or no trust, health information has only a slight or even a negative effect (366).

Qualitative data describing health education illiteracy in this population, for example about the importance of adherence to ART and protected sex, are concerning. These findings suggest areas for improvement in the use of peer support and the need for communication skills training for staff in the standard care clinic.

7.3.1.2. Medication and symptom relief

Quantitative analysis of data regarding service receipt found a statistically significant difference in the receipt of weak opioids (codeine) between study arms. This may suggest that pain is less well managed in the standard care clinic. Receipt of paracetamol was associated with benefit in all quantitative outcomes, indicating that the availability of non-opioid analgesia is essential to holistic health.

The qualitative data described how analgesia adequately relieved pain for the majority of participants, which alleviated the associated fear and anxiety that their distressing physical symptoms would never be resolved, and that they would not be able to work or provide for their families in the way they wished.

These findings suggest that a more consistent prescription of mild opioid analgesia would be beneficial for relief of pain and holistic well-being, in line with the WHO recommendations (385). A recent pharmacy stock audit of 120 PEPFAR funded health centres in East Africa found that 73% were well stocked with non-opioid analgesics (suggesting that 27% were not), 21% had codeine and only 7% of pharmacies were stocked with strong opioids (386). In the same study, of the pharmacies who reported that they did stock these medicines, stock-outs were common, with 47% reporting stock-outs of non opioid analgesia tablets, 33% reporting a stock-out of weak opioid tables and 100% reporting stock-outs of strong opioids (386). This suggests that even when prescribed, problems in the supply chain mean access to adequate pain relief may continue to be a problem.

Lack of consistent access to analgesia and other medications for symptom control is an additional barrier to improvement in mental health and well-being for PLWH in this context. Introduction of the WHO pain ladder as a widely used and inexpensive approach to pain management should be made routine (385), in addition to improvements to the supply chain to prevent stock outs of essential medicines.

7.3.1.1. Time to talk and articulated concerns

Analysis of quantitative differences determined that study participants receiving the intervention care package received more psychosocial care than those in the standard care arm. Psychosocial care included emotional support for the individual and their family, and time to discuss concerns, spiritual worries and planning for the future. Qualitative data analysis showed how having time to talk about their problems was extremely important for therapeutic benefit reported by those receiving the intervention, and was notable in its lack when they returned to standard care.

Psychosocial care is neglected in many healthcare settings internationally, despite its importance for patients. A recent RN4cast study of nursing levels and their implications on care quality and safety was conducted in the UK and in eleven other European countries (387, 388). The UK research findings showed that due to a lack of time 87% of nurses omitted certain essential nursing tasks, most frequently those related to psychosocial care. Comfort care or time for patients to talk was omitted by 66% of nurses in the UK and 53% of nurses across the other European countries (387, 388). The high levels of unmet need at baseline in this study (

Figure 16, Page 124) indicate that there are significant unmet psychosocial needs in this sample. This potentially indicates a routine neglect of psychosocial care in the standard care clinic. In conjunction with the RN4cast data, this demonstrates a pattern of inadequate provision of psychosocial care across international settings. The evidence suggests that a lack of time to interact with patients may be an important constraint (388).

Evidence suggests that when time is constrained, nurses prioritise medical tasks to process patients through the system to prepare them for medical discharge (388), most clearly seen when staffing levels are low (387). As the standard care clinic is extremely busy (400 patients/ day, see Table 3-1, page 56), it is likely that the neglect of psychosocial care is due to increased workload and subsequent time constraints.

Another explanation for this neglect of psychosocial care is the lack of importance placed on holistic well-being by health care professionals working in the standard care clinic. A study from the UK found that when patients in primary care presented with unexplained physical symptoms and even when they suggested potential psychosocial causes, GPs were preferentially more likely to suggest physical investigations and interact with a low level of empathy (389). These findings suggest that even when patients present with physical symptoms recognised as expressions of unmet psychosocial need, they are not managed appropriately and referred to appropriate care, even in a relatively well resourced healthcare setting of a UK GP practice. As discussed in the background

chapter of this thesis, nurses trained in Kenya receive a comprehensive training package, including training on chemistry, microbiology, haematology, anatomy and pharmacology, in addition to sociology, psychology and hospital and community nursing (194). However, this comprehensive course, while commendable, neglects communication skills, person-centred care and the importance of managing the holistic experience of illness, focusing instead on diagnosis and management of disease. This focus on medical management in nurse training does not appear to prepare nurses to care holistically for their patients.

The evidence base for the effectiveness of psychosocial support in the management of physical outcomes in chronic conditions is established and psychosocial support is now mandated as part of supportive cancer care (390, 391) and coronary care (392). The findings of this study indicate that psychosocial care and support is unacceptably under-addressed in the care of PLWH.

7.3.2. Therapeutic aspects and processes of participation

7.3.2.1. Compassionate care, social support, communication and trust

As described in section 6.4.3.1, trust can be seen as the therapeutic process associated with compassionate care, social support and communication. In this section each therapeutic aspect will be discussed with reference to the wider evidence, and then the proposed interactions between these aspects of the study and trust, to suggest a theoretical process facilitated by trust which led to improved mental health and well-being.

Compassionate care

The Latin origins of the word compassion are to “suffer with”, expressed by those who are witness to suffering, and through this experience of ‘being with’, feel motivated to alleviate the pain they witness (393). A definition from the nursing literature states that: “compassionate care is an interaction in which one person recognises and responds to the need or suffering of another by giving physical or emotional comfort” (394). Suffering can be physical, social, psychological or spiritual in nature.

Participants in this study described experiencing the study team’s compassion, and the positive effect that this had on them during their participation in the study. They described being treated well: with respect and dignity and with attention to their personal needs and wants, including the need to be known by their health care provider.

Participants described a lack of a compassionate approach in the standard care clinic, which is not unusual in health care systems under pressure to deliver care to high numbers of patients. A study in a paediatric ward in Tanzania implemented an intervention to improve relationships between staff and parents (395). The study reported that despite much effort on the part of the ward staff, relationships did not significantly improve, owing to systemic problems in the working environment: poor inter-staff relationships and low responsiveness of the hospital management to their complaints and difficulties at work (395). Participants in a study from Nigeria, Tanzania and Uganda reported that harsh, uncompassionate treatment from staff was a common reason for HIV patients non-attendance at clinic for appointments, leaving patients feeling angry, humiliated, and disengaged from treatment (396).

“Being known” was an expression of compassion important to many participants. They felt cared for when the study team knew to ask about their family, or remembered important things about them such as their previous health complaints. A qualitative study of communication needs in breast cancer patients found that patients wished their doctors to know them as individuals, which often meant having a conversation about something unrelated to their diagnosis (such as family) or making the patient feel special in another way (397). Patients with breast cancer in a Canadian phenomenological study described being known as key to building trusting relationships with their physicians, which was found to be essential in countering feelings of vulnerability associated with illness and expressed by all patients (398).

Facilitators of and barriers to compassionate care in healthcare were reported in a review published by the Kings’ Fund in the UK in 2009 (393). The authors identified dealing with and preventing staff stress and burnout and ensuring support from the wider organisational structure of hospital care as ways to encourage compassionate care (393). More recently, Watters *et al* conducted a qualitative enquiry into the presence or absence of compassionate care as experienced by patients and staff in the healthcare setting (399). They identified that compassionate care was facilitated by effective and supportive inter professional teams, role modelling by other members of staff, personal factors such as beliefs values and compassion capacity, high nurse-to-patient ratios and supportive managers who are aware of individual staff needs (399). Barriers to compassionate care were a high workload, personal factors such as fatigue or stress, managerial requirements such as audit and meeting targets and variance from normal care pathway (399). These findings support the evidence from Tanzania cited above, that managerial support is essential to creation of a compassionate care culture in healthcare (395).

Compassionate care in the standard care clinic was notably lacking when compared to the participants' experience of the intervention and engagement with the study team. Evidence suggests that receiving compassion is associated with a reduction in anxiety and improvement in mental well-being (225) in addition to improved control of diabetes and cholesterol and increases in patient and family satisfaction (400).

It is possible that the lack of compassion observed by participants was due to lack of time available for clinicians and the lack of support from management, to take time to provide this care. However, studies have shown that compassionate care is being delivered in similar clinical environments in SSA. In a qualitative study of staff and patients in rural clinics in rural Zimbabwe patients described staff as friendly and reported that staff listened to them, acknowledging that their HIV was "more than a medical condition" (401). This was reportedly extremely therapeutic.

Expressing compassion, whilst a normal human response, is described as a potentially painful experience for the person expressing compassion, as they 'suffer with' the sufferer (393). This highlights the need for support for staff in order to facilitate the provision of compassionate care. Time is required to be compassionate, which requires support, commitment and role modelling from high level management, and reductions in staff workload to prevent stress, fatigue and burnout (393).

Social support

Receiving compassion from the study team built trust in their relationship with participants, which was perceived and described by participants as a source of social support. Findings further suggest that this support encouraged participants to build relationships with their peers and participate in religious practice in a way they had previously been unable to do, and from which they also gained therapeutic benefit. Participants described receiving social support from the study team and seeing them as friends, with a mutual exchange of affection. They described disclosing their status to peers, exchanging peer support and engaging with religious practices, all of which were associated with improved mental health and well-being.

These findings are mirrored in the extensive literature on social support and mental health and well-being. Kaplan et al, in their seminal paper on social support and health(402), summarise evidence which suggests that a perceived lack of social support or any change or decrease in social support can result in psychological, and in some cases physical ill health. They describe how having adequate social support enhances self-esteem and provides affirmation and a place to express negative

emotions (402). High levels of emotional and tangible social support have frequently been found to be associated with low levels of depression and anxiety (382).

Communication

Participants expressed the importance of openness in interactions with the study nurses and researcher. They spoke of feeling free and being interacted with in a free way, which encouraged them to respond in an equally free and open manner. They also reported disclosing to others after speaking to the research team, potentially an effect of being empowered by this positive experience of talking openly and without shame

It is likely that the researcher emphasised the importance of talking freely for data collection. It is essential that the interviewee understands that information that they might wish to convey is acceptable and interesting to the researcher, who works to create an atmosphere of openness and acceptance where interviewees do not fear judgement when disclosing their personal, intimate experiences (403). In an attempt to reduce interviewer bias, researchers in qualitative research are advised to sustain a “empathic neutrality whereby the researcher uses personal insight while taking a non-judgemental stance” (403). To a stigmatised and marginalised individual, it is possible that this message could be read as, ‘my experience is acceptable and therefore I am acceptable’. In this way, the research process contributes to the feelings of increased self worth and acceptance reported in the qualitative data.

The interaction between researcher and interviewee, described as free communication and non-judgemental acceptance has similarities with the concept of positive unconditional regard described by Rogers *et al* (404), in which therapists are encouraged to express neither approval nor disapproval, simply acceptance. Rogers describes unconditional positive regard as essential for therapeutic personal change. The trust built through the therapist’s unconditional positive regard of a client seems to have also been built during the study between researcher and participant, with therapeutic consequences.

Effective and sensitive communication could have implications for holistic well-being; due to both the way in which information was given and the benefit of the information itself. Participants in this study described the positive effects of being listened to, and sharing their burdens with the researcher on their mental health and well-being. The work of Payne *et al*, exploring communication and in primary care, found a positive approach such as that demonstrated by the study team, was associated with patient satisfaction (196). Similarly, in a recent systematic review, high quality communication between physician and patient was found to positively influence emotional health,

resolve symptoms, improve function and pain control (405). When functionally and subjectively measured, skilful quality patient physician interaction which increases patient control and includes positive affect and health information has been found to be associated with better health status (406).

It is apparent in the findings of our study that participants felt too unsafe to discuss their problems amongst their community. Similar findings have been reported from a study of PLWH in South Africa, which identified the need for a safe forum where PLWH could exchange information about how they could apply health information to their lives, within the context of a stigmatising condition (167). Participation in our study created a similar space and opportunity to reflect on the experience of living with HIV. Campbell *et al* suggest that reflection and review, create the beginnings of critical thinking and facilitate the shift from victim to empowered actor, and help PLWH to develop the confidence to engage with and positively influence their environment (165, 167).

That the high quality communication skills of the study team enabled participants to express themselves freely, which was therapeutic in itself, but also created a therapeutic relationship, in a similar way to unconditional positive regard, and positively influenced mental health and well-being, through increases in patient control (section 7.3.2.2, page 221) and the provision of health information (section 7.3.1.1, page 213).

The therapeutic process of trust

Whilst it is apparent that compassionate care, social support and communication were therapeutic aspects of participation in the study, it is essential to understand why this was the case. I believe that these aspects of participation were therapeutic because they enabled trusting relationships to be formed, within which participants were able to rebuild their self image and improve their mental health and well-being.

Trust in relationships with healthcare providers was examined in a qualitative study of patients with chronic conditions (Lyme's disease, breast cancer and mental illness) (407). Study findings showed that expressions of caring, concern and compassion were the most important aspects of a trusting relationship, with listening as centrally important (407). Provision of emotional support (defined as demonstrations of love, caring, esteem and value, encouragement, empathy and sympathy) has been postulated as the mechanism through which social relationships enable the distressed person to express their emotions, and have their feelings validated, thereby bolstering self-esteem (408). It is suggested in the literature that peer support is particularly important for offering relevant and appropriate coping assistance and supplying advice, appraisal and feedback, as an individual's hope

increased with the knowledge that there were others who have coped successfully (408).

Participants in this study described the study team as friends, which implies that they saw them as peers to some extent, which may in turn explain the extent to which social support was received through participation in the study.

Participants also described how aspects of participation in the study built trusting social relationships, first with the study team, and then beyond. There is evidence that trust may be the key to accessing support from pre-existing social networks. A study conducted by Grace *et al* into social support in undergraduate students describe reliance on social support as dependent on levels of interpersonal trust, where those with high levels of interpersonal trust perceive more social support from friends and family, and use these sources of support to withstand stressors (409). Those with low levels of interpersonal trust were more likely to use maladaptive coping such as avoidance or substance abuse.

This evidence suggest that in fostering trusting relationships, through compassionate care, communication and the provision of social support, further support was accessed, which decreased the use of more negative coping mechanisms such as avoidance and isolation, and improved mental health and well-being.

7.3.2.2. PROMs as prompts and self-care

During the study participants described how they used the PROMs as a prompt to self-care, suggesting that the PROMs exert their therapeutic benefit through reminding or highlights actions which could promote health that the participants could engage in, or areas of well-being which the participants had not before considered, which they subsequently reflected and then acted upon. This was explicitly described by participants in areas such as protected sex and medication adherence, where responding to the PROMs was used to identify gaps in health education which acted as a catalyst for behaviour or attitude change.

The increased motivation for self-management is encouraging, particularly as HIV transitions into a chronic condition, in which patients are required to adhere to medication, adapt their behaviour in response to symptoms, adjust to social and economic consequences and interpret and manage their symptoms for the rest of their lives (410). It is recognised in the literature that patients with chronic conditions need increased access to appropriate health information including information on diagnosis and implications, treatments and consequences, potential impact on their future, sources of support, and coping and adjustment strategies, to enable them to manage their condition (410). This suggests that as HIV becomes increasingly recognised as a chronic condition, care may shift to

one of shared responsibility, based on patient need, and suggests a patient centred approach, with a sense of ownership and control will be necessary. This approach has been adopted in the management of chronic conditions such as diabetes, hypertension and angina (411-413).

The unanticipated therapeutic benefit of completing the PROMs indicates that patients are able to recognise, and when promoted, address the gaps in their knowledge of HIV and healthy lifestyles. Some participants also benefited from having a forum or structure, from which they were able to reflect and take steps to manage their own mental health and well-being. Finally, these results highlight the potential use of a simple short tool to have significant therapeutic benefits, which could be used to increasingly empower PLWH to manage their condition.

7.3.2.1. Material support and relief of financial strain

Findings from the qualitative analysis suggest that material support in the form of light refreshments and financial reimbursement for travel expenses relieved anxiety for participants in both the control and intervention study arm.

One possible causal mechanism for this observable effect is the relief of economic hardship. Participants described how they were able to purchase item they would otherwise have not been able to afford. It is difficult to extract whether the relief they reported was simply because they didn't have to worry about these things anymore, or because the extra financial support meant that they had more of a sense of personal control, which we know from the literature is associated with self-esteem and mental health and well-being. This effect has been shown in research from New Zealand (77), China (414) and the USA (79). In the USA, personal control was found to mediate the relationship between financial stress and chronic poor health, depression and reduced social and emotional functioning (79). Research conducted among older African-American people with HIV found that financial strain was a significant predictor of life satisfaction (415).

Another potential causal mechanism for this effect is the sense of care and belonging that the material support engendered. Similar findings have been reported in an anthropological study of financial reimbursements for research participants in Kenya (416). Participants reported that the tangible material transfer made them feel cared for, in a similar way to the participants of our study. Findings of the anthropological study described how being in a research study made participants feel they belonged with or were being taken care of by the research foundation, and led to a sense of attachment and care which improved their mental health and well-being. The authors suggest that "monetary transactions and other transfers of material value are experienced as part of wider connections and collectives, larger possibilities and hopes" (p.53) (416).

7.3.2.2. The effect of therapeutic processes on stigma and shame

Participants in this study described feeling shamed, socially isolated and in some cases suicidal due to the HIV-associated stigma and discrimination they experienced. The building of trust between participants and the study team appears to have counteracted this shame by verbally and non-verbally normalising the diagnosis, and teaching the participants that they are worthy of being treated with dignity and respect, and should therefore treat themselves as well.

Internalised stigma, where the socio-culturally sanctioned stigmatising messages are incorporated and accepted by the stigmatised, often manifests as shame (70, 417-419). A definition of shame has been generated from evidence from women in the USA who describe it as: “An intensely painful feeling or experience of believing we are flawed and therefore unworthy of acceptance and belonging” (420).

Some participants described how during the study they became more able to resist shame and stigma and discrimination, either passively or actively. As described in section 6.3.2.4, participants who had previously isolated themselves to avoid discrimination began to reject these stigmatising messages. This occurred internally at first as participants acknowledged privately that messages of immorality or dirtiness were untrue. Increasingly, some participants began to engage with the community and not avoid contact with those they thought may discriminate or stigmatise them. The full extent of this resistance was reported by participants who described challenging those who expressed discriminatory views, and in some cases forging a new role of HIV activist in their communities.

Participants had difficulty identifying what it was that catalysed this change. They described the change in their behaviour as due to something which occurred during the interactions with the researcher during data collection and with the study nurses during receipt of the intervention. The data suggests that these interactions, through the building of trust, somehow enabled participants to rebuild their self-image, which had been eroded by stigma and discrimination, and thus reject the stigmatising messages.

The theory of shame resistance developed by Van Vliet contributes to an understanding of how participation in the study could have led to an increased resistance to stigma (421). The theory was developed using a grounded theory approach, with data from adults in Canada who had experienced and partially overcome a significant shaming episode (such as being caught and convicted of shoplifting or being accused of rape). Van Vliet describes five processes through which resistance

occurred: connecting, refocusing, accepting, understanding and resisting (421). I will now discuss these processes with reference to the findings of this study.

‘Connecting’ describes the movement from social isolation to connection. This involves finding allies who can be supportive, socialising with others through participation in community activities, talking with others (particularly about experiences of stigma and shame and being accepted and normalised in this), connecting to a higher power and repairing relationships (421). In the current study the first allies were the study team, who were able to talk with participants, and provide a forum within which participants could express themselves without judgement (therapeutic aspects of social support and communication see section 6.4.3.1).

‘Refocusing’ describes shifting energy and attention from the source of shame or stigma to personal goals and self care behaviours, focusing on personal strengths and qualities, and working on self improvement. Participants reported increasing self care during the study, often prompted by use of the PROMs during data collection. They also described shifting attention from others to themselves, and learning to ignore those who wished to talk and gossip about them.

‘Accepting’ involves a move from avoidance towards facing the reality, including acceptance of one’s feelings and expressing them (421). Participants often spoke about the importance of accepting their diagnosis and their situation, partially associated with receiving normalising messages from the study team. They also benefitted from communicating their feelings (sharing burdens for relief see section 6.4.3.1).

‘Understanding’ refers to learning about external factors such as extenuating circumstances and separating from shame and developing insight into the underlying reasons for one’s actions and behaviours (421). Participants demonstrated this when they described how they had come to realise that anyone could become infected with HIV, and that it was normal, and therefore acceptable.

The final process is ‘resisting’, which concerns the rejection of stigmatising or otherwise negative judgements and asserting and challenging those who persist in those judgements (421). This is most clearly described by the participant in the control group (ID 143) who moved from discrimination victim to activist, bringing people who had discriminated against her into the clinic for HIV testing. Other participants described resistance in more gentle terms: reaching out to family members who had previously rejected them, deciding not to be ashamed, disclosing their HIV status to the community, and offering to be a support to those newly diagnosed. This resistance describes the forging of a new identity as an HIV positive person in society, without shame, whether as an activist

or as a normal person who interacts with their immediate and local community, regardless of the discrimination or stigma they may face.

This phenomenon of forming a new identity is also described in the work of Soskolne, who conducted a narrative analysis of the life stories of HIV positive women in South Africa (422). The author describes how the women who were more resistant to stigma had negotiated a new, positive self identify, which helped them cope with stigma related anxiety (422). A qualitative inductive exploration of illness narratives and adherence among PLWH in South Africa suggests that adequate practical, emotional and social support is essential for individuals to forge new 'stigma resistant' identities (423). These narratives revealed how participants required a sense of being valued or supported by others in order to forge a new identity which empowered them to manage the stigma they were facing (423). With wider support, PLWH were able to express their emotions, make sense of their diagnosis and move towards a problem solving approach toward managing their health, whereas those with fewer social and emotional resources were less able to adjust and cope (423).

Evidence from the literature and from this study suggests that if PLWH are provided with social (social support), emotional (compassionate care, time to talk) and practical support (material support) they may be able to resist HIV-associated stigma. This has resonance with Van Vliet's model of shame resistance.

7.4. Summary of therapeutic benefit

The intervention care package had a statistically significant effect, improving psychological quality of life, psychiatric morbidity and ability to share feelings with friends and family, compared with standard care. It did not have a statistically significant effect on the extent to which participants worried. Longitudinal summary measures showed that those with higher levels of education demonstrated poorer psychological quality of life, lower levels of ability to share feelings and increased psychiatric morbidity over time, and those with higher levels of wealth reported higher psychological quality of life and lower psychiatric morbidity over time. Men also reported improved ability to share over time.

Active ingredients of the intervention were identified as insight and understanding, medication and taking time to talk, with the associated mechanisms of action of adequate information, symptom relief and articulated concerns. Therapeutic aspects of participation in the study were identified as compassionate care, social support, therapeutic benefit of talking, PROMs as prompts and material support, with their respective processes of trust, self care and relief of financial strain. These ingredients and aspects contributed to positive mental health and well-being.

Unmet physical, social and psychological needs were identified as barriers to therapeutic benefit. Many participants receiving standard care reported that nursing staff did not have time to talk to patients about their concerns and problems, which often remained unaddressed. Increased allocation of time may result in the alleviation of these concerns and problems, but further research is warranted to explore how to better meet patients' needs in standard care.

Based on Table 1-5, created to summarise the evidence in the literature for the effectiveness of aspects of palliative care interventions on mental health and well-being, the contributions of the findings from this study are summarised in the same way in Table 7-4, for the effectiveness of palliative care for PLWH.

Table 7-4 Summary of evidence for the effectiveness of nurse-led palliative care intervention

Component of palliative care	Evidence from this study for effectiveness of palliative care on mental health and well-being	
	Findings from quantitative data analysis	Findings from qualitative data analysis
Symptom management	Receipt of codiene associated with increased odds of reporting high ability to share. OR 4.46 p= 0.01	Active ingredient: Medication
Patient and family support: psychological, social or spiritual	Findings reported in Table 6-19 indicate that almost all participants in the intervention study arm received emotional support for themselves and their families	Active ingredient: Insight and understanding Time to talk
Illness understanding and patient education	-	Active ingredient: Insight and understanding Time to talk

Within the context of an environment designed to promote well-being, patients with extraordinary needs cannot be satisfied with standard medical and nursing care. In this respect, it appears that the experience of receiving palliative care for PLWH in Kenya is similar to that of other patients receiving palliative care in other countries and contexts, as described by patients receiving specialist palliative care in the UK in the work of Jarrett, Payne et al, who reported that the most valuable aspects of receiving palliative care were pain control and someone to talk to (424).

7.5. Study reflections

7.5.1. Sample characteristics

Table 5-5 describes the sample characteristics for the TOPCare trial phase 1 data. This sample is younger than the usual palliative care population, and is 81% female. Whilst this is not usual for a palliative care sample in HIC, it does reflect the epidemiology of the wider HIV pandemic, particularly in LMIC. Those infected are usually young, and female (29).

In addition, participants report a median of 2 children and 3 financial dependants. This indicates that they have responsibilities to provide for people beyond their nuclear family. Whilst this is usual in Kenyan society, it is worth bearing in mind when considering the importance of social role to mental health and well-being in the findings of this study. Participants knew that if they were unwell or otherwise unable to provide, there would be a wider network of dependants who would also suffer. In light of this, it is unsurprising that social role was so integral to positive mental health and well-being.

7.5.2. Reflections on the framework of mental health and well-being

The framework for mental health and well-being in this study was developed by the WHO, University of Melbourne and VicHealth in Australia (section 1.2.2, Pg. 28). This framework described the determinants of mental health and well-being as social inclusion, freedom from discrimination and violence, and economic participation.

This thesis has found further evidence for social inclusion as a determinant of mental health and well-being. Social support from the study team, peers and religious practice were reported as a therapeutic aspect of participation in the study. Supportive relationships were described by many participants as extremely important, where they could rebuild self-image and personal strength.

The second determinant described was freedom from discrimination, which includes physical security, self determination and control over one's life. As participants progressed they were able to resist HIV-associated stigma, ensuring their physical security, which occurred in parallel with reports of improved mental health and well-being. There were anecdotal reports among the intervention arm participants that receiving couples counselling from the study nurses reduced incidence of domestic abuse, although this was not an active line of enquiry during the study. In addition participants reported that material support increased their ability to contribute and provide for their family's' needs, increasing their sense of control over their lives, and thus improving their mental health and well-being.

Economic participation is the final determinant of mental health and well-being including the importance of work, education, housing and money. Work, education housing and money were extremely important to our participants, potentially because they lived in the context of poverty. Participants expressed gratitude that the intervention improved their well-being such that they were able to work, and earn money, which improved their mental health and well-being.

The findings from this study support and extend the use of the VicHealth framework for understanding mental health and well-being, and its promotion among this sample.

7.5.3. Methodological limitations

There are several possible limitations to the findings of this study, each of which will be discussed in turn.

7.5.3.1. Missing data

All participants who left the study before the end of the trial period were in the intervention arm of this study. Whilst this has been explored in great depth in section 5.1.2, it would be remiss not to reflect on it at this point as a potential limitation.

Field workers from a study conducted in Kenya reported finding it highly distressing to follow study protocol in the absence of the people who wrote it (425). They described ethical dilemmas, where they were required to withhold care from patients in need, in order to comply with standard operating procedures, increasing the temptation to provide care whilst knowing that this would compromise the study (425). We anticipated these dilemmas, and the pressure on the researcher, particularly at the point of randomisation. The researcher and I discussed in person how important it was that the randomisation was conducted correctly, and the implications for the data and future research if it was compromised. However, it is impossible to be certain without being present that the randomisation was not compromised, and visibly sicker patients who subsequently died preferentially allocated to receive the intervention.

At the present time, based on a full investigation of the available data for each person, the research team as a whole is accepting that this occurred by chance, but should this not be the case, it would have implications for the validity of our findings.

7.5.3.2. Inability to analyse APOS worry item

Due to the data type and distribution of the AUC for the APOS worry item, it violated the assumptions of linear and ordinal regression models, and therefore could not be analysed. This means that I was unable to test for any association between worry over time and demographic and clinical variables.

7.5.3.3. High ineligibility rate

Of the total sample of patients screened for inclusion in the study, 16.2% of patients were stable on ART and reported pain or physical symptoms scored at 3 or above on the APOS and therefore were eligible for inclusion in the trial. For all patients, including those where were not on ART, this figure decreases to 13%.

These findings of this study can only be extrapolated to PLWH with moderate to severe unresolved pain or other symptoms. The eligibility rate indicates that this is a relatively small group of patients. Had the eligibility criteria more closely reflected the holistic nature of palliative care, and screened for the presence of social, psychological or spiritual problems, the eligibility rate may have been higher, and may have more closely reflected the need for holistic care in this patient population. Informal communications with the study nurses, who have extensive experience of working with this population, indicate that this would be the case.

7.5.3.4. Refusal rate

The refusal rate (55.72%) appears to be relatively high compared to studies in similar populations in Sub Saharan Africa (30% (426), 12% (427), 3% (428)). A study conducted in the same region of Kenya as the current trial explored the concept of informed consent in a trial with 100% consent rate (429). They conclude that many participants consented to participation due to fears of inferior treatment if they refused, or because they assumed that there would be direct therapeutic benefit, despite the randomised controlled trial study design (429). This paper also reported that if potential participants refused to participate, often it was because they anticipated little personal therapeutic benefit for the personal cost to them, either financially or in time (429). In the light of these findings, our comparatively high refusal rate of 55.7% may not be a cause for concern.

This refusal rate should also be examined in light of the fact that the researcher in the TOPCare study was instructed to guide the participants through the information sheet slowly, answer questions and specifically advise participants that there would be no consequences to refusal to

participate. A report into informed consent for a diabetes clinical trial in the Navajo tribe in the USA revealed that, counter-intuitively, careful explanation of the risks and benefits designed to increase trust in the research process was in fact associated with increased mistrust (271). The extent of the detail of the discussions with the research team in this case reportedly lead to embarrassment and confusion on the part of the tribes' people and contributed to a high refusal rate (271). It is possible that the highly detailed, careful approach to the consent process affected prospective participants in this study a similar way, which could partially explain the increased refusal rate. It is also possible that due to the clear explanation to participants at consent, participants were aware of the costs to them and therefore did not consent if they would be unable to attend and participate fully in the study.

The researcher was also instructed to explain clearly that should the participant be randomised to the control arm, they would continue to receive the same care in the clinic as previously but would be expected to attend five data collection interviews, each lasting approximately 45 minutes. Participants had a good understanding of the costs and benefits of participation, financial and otherwise, and the very real possibility that they may not receive the intervention. Informal data gathering by the researcher suggests that the majority who refused to participate were dissuaded by the time commitment required, because they would be unable to take time off work to attend the appointments. This is also supported by the minimal attrition rate, which suggests that those who consented to participate were aware of the demands on their time and were able to fulfil them.

It is possible that the participants felt that this research was too costly, either in terms of time taken, financially due to missed work opportunities or emotionally due to the sensitive nature of the subject. Respondent burden is defined as a subjective phenomenon of physical, psychological or financial hardship associated with participation in research (430). It is more problematic in situations where questions may be sensitive, stressful to answer or the process could be demanding in terms of interview time or frequency. It is important to bear in mind that this study was conducted in an outpatient setting, and the patients in this population have roles and responsibilities to fulfil outside of the study setting. Research fatigue has been found to be associated with a lack of practical change seen from previous research engagements (431). The study site for this trial is very experienced in conducting research and it is a possibility that this population are research experienced, increasing the chance of respondent burden or fatigue. Unfortunately no data were formally collected on reasons for refusal to participate.

A study in Ethiopia exploring the process of informed consent found that having a stigmatising condition reduced the likelihood of consent, as participants feared further stigmatisation as a result

of their participation (432). As HIV is a stigmatising condition, it is likely that this contributed to refusal for some potential participants.

Finally, in interviews for phase 2, participants were asked why they consented to participate in the trial. Most participants interviewed for phase 2 reported that they consented because they wanted to be helped. It is possible either that those who refused were not experiencing the same level of need, or that those consenting had very high levels of need. Therefore, the refusal rate may impact on the quality and generalisability of the findings because those who refused to participate were different to those who participated. Those who consented did not perceive that the demands made on them by their roles and responsibilities prohibited them from participating in terms of time, and therefore may have been less socially connected, less physically able or different in other ways associated with taking on responsibility, or may not have been in paid employment as much. Those who consented also had high levels of need and wanted to be helped, which may not reflect the nature of the wider clinic population.

Should this concern be justified, then in a sample with less need at baseline, who were working and therefore less financially constrained, and with more social responsibility and therefore less socially isolated, the effect of the intervention may have been not as strong, or even detectable.

In summary, the refusal rate may be a positive reflection of the extent of the information given prior to consent, which meant potential participants were able to make an informed decision about their participation. Other contributing factors could be research fatigue, respondent burden, or the stigmatising nature of HIV. There is however evidence to suggest that those who refused to participate may be different to those who consented, indicating further constraint on the generalisability of findings.

7.5.3.5. Cross cultural research

International best practice in cross language research includes back translation of any translated documents to verify internal validity, ensuring that concepts which may be difficult to translate, especially culturally bound concepts such as mental health and well-being, are accurately conveyed in the translated versions (293). Due to time and logistical constraints, back translation was not undertaken. This may have introduced some systematic bias and reduced the internal validity, as we cannot be sure that the concepts described were well understood by participants completing the measures.

In addition, 27 qualitative interviews were conducted in Kiswahili, transcribed and translated into English for analysis. It is important to acknowledge that some detail, nuance and inflection may have been lost in this translation, in addition to the cultural distance between participants and me as the analyst. This cultural distance means that I may have misinterpreted the data. According to Ingvarsdottir *et al*, the process of translation includes three 'coherence systems', or means for understanding and constructing accounts: those of the researcher, the participant and interpreter. Whilst on a verbal level there may appear to be agreement and comprehension, it is impossible to be sure that there is concordance between all three parties (433).

The challenges experienced when collecting and analysing data in a different language are similar to those experienced in secondary data analysis, primarily because of the cultural distance between myself as the analyst and the researcher (274). Temple *et al* suggest that interviews conducted in the physical absence of the analyst, and in a language that the analyst cannot understand, are actually 'third hand data' (274). This may mean that the data lose meaning or are contaminated with unjustified interpretation as they undergo collection, interpretation and analysis processes.

In addition, in a similar way to secondary data analysis, during data collection the analyst cannot influence the interaction between researcher and participant, and is not as involved or situated within the social context of the research participants and data collection (274). This may limit the lines of enquiry available to the analyst, and inductive themes which emerge may not be able to be fully explored, suggesting that the findings may not be complete.

To mitigate for these effects, I presented initial findings to the Kenya study team, senior hospital management and 80 of the 120 participants who were contactable six months after data collection closed (section 4.4.3). This was done using a power point presentation, translated into Kiswahili by one of the study nurses. The participants then asked questions and commented on the findings. This was primarily a dissemination exercise, to feedback the preliminary findings to participants as a sign of our respect for the participants and the time and effort they put into sharing their experiences with the study team, but it was also to verify that the preliminary findings were consistent with their experiences. Feedback was extremely positive. Participants communicated how much they appreciated participating in the study with the senior management of the hospital and with the research team from the UK. They asked that the study continue and be made available for all patients in the standard care clinic. They also asked for more opportunities to talk and for more peer support groups to be formed to support them in this way.

7.5.3.6. **Transferability of findings**

There are two difficulties with the transferability of these findings. Firstly, this trial tested a palliative care intervention, for which experience of chronic pain or symptoms (more than 2 weeks) was used as an indication of palliative care needs and thus eligibility. This cut off was used because the primary outcome of the trial was difference in pain; therefore participants with pain were recruited to the trial. This is a limitation of the findings in terms of transferability to other HIV positive populations who do not have unmanaged pain or symptoms. The 16% eligibility rate for this trial from in-clinic screening indicates that the findings may not be transferable to the remaining 84% of patients who did not have severe to moderate pain or symptoms.

As previously mentioned, if eligibility for palliative care was defined in this study based on less biomedical criteria, it is anticipated that more patients would have been eligible, as the study nurses recognised that many patients with or without pain or other symptoms experience social and psychological distress. This suggests that the findings may be more transferable than it initially appears, although this warrants further investigation.

Secondly, the trial was conducted within the context of a country with an established palliative care movement. As previously reported, Kenya has been rated 4a by the International Observatory of End of Life care, which means that palliative care services are relatively well developed and are beginning to be integrated into mainstream services (26). This highlights the limitations of the findings in terms of transferability to other countries without similarly well developed palliative care services, or other holistic care options. Countries such as Mozambique, which reported a HIV prevalence of 11.1% in 2012, and only isolated provision of palliative care might struggle to see similar results without the wider support of local expertise in palliative care developed over the past decades in Kenya (26, 29). Should this study be replicated in such an environment, it would be possible to identify the contribution of the palliative care infrastructure on the outcomes we observed, beyond the holistic philosophy of care.

7.5.3.7. **Regression toward the mean**

The participants recruited to the TOPCare study were recruited on the basis of them reporting a pain score of at least 3 on a scale of 0-5. This relatively high level of pain or symptoms is likely to be associated with some level of psychological distress, as is well documented in the HIV literature (223, 434). Therefore, if the sample began with higher than normal levels of psychological distress, it is

reasonable to assume that this sample would experience some improvement in mental health and well-being due to regression to the mean, and not necessarily due to treatment effect.

Regression to the mean is a statistical phenomenon which describes change in observations from the same individual which are not due to the effect of an intervention, but due to natural change over time because of the extreme value of the first observation. Extreme values are described as such because they are unusual in the population, and will be therefore caused by a rare combination of factors, which due to their rarity, may not occur again in the same combination (435). If the two observations taken from the same individual were uncorrelated, we would expect the second observation to be much closer to the population mean, but as these measures are correlated, because they are from the same person, the change is less but the direction the same, towards the mean. The further the observation is from the population mean, the stronger the effect of regression toward to mean (435).

To assess for regression to the mean, I compared the data from this study with similar dataset from a three month observational study in Kenya of 696 participants taken from PEPFAR funded clinics, who reported pain and symptoms on the APOS in addition to the MOS-HIV (331). MHSS data from this study for the participants reporting a pain score of 3, 4 or 5 at baseline (n=151) reported a mean change over the observation period of 11.32 MHSS points, which is greater than the 10 points which denote clinical significant change (307) . This suggests that these patients improved over time without a specific intervention for their mental health and well-being, due to regression to the mean, or other unmeasured contextual factors. (These patients received clinical management of their HIV (99%), a package of health promotion for people living with HIV (94%), with less reported receiving psychological support (58%) (331)).

Mean change in the TOPCare study was 10.32 MHSS points in the control study arm and 12.41 in those receiving the intervention care package. If we assume that the difference seen in the PEPFAR data is due to regression towards the mean, in the absence of any other explanation, we must also attribute some of the change seen in the TOPCare study data to regression towards the mean. However, for the TOPCare study data we have data from mixed methodological approaches, which provide evidence to suggest that although the effect seen may be partially due to regression to the mean, it is also due to the therapeutic aspects of study participation (section 6.4.3).

7.5.3.8. Other possible sources of bias

Trial effect

Therapeutic benefit from participation in a trial is a recognised phenomena, and one of several referred to in the literature as the Hawthorne effect (436). Therapeutic benefit from participation indicates that participation in a trial improves outcomes for both control and intervention study arms, caused by environmental factors such as a study team with a compassionate approach, a sense of participation in something important, or pride in being chosen for a research project (436). This effect has been identified in medical, education and management research (437, 438).

It may appear that the sample for the TOPCare study experienced the Hawthorne effect, as participants reported improved outcomes in control and intervention study arms. However closer examination of the qualitative data revealed that the therapeutic benefits described could be attributed to specific aspects of study participation, and not simply due to feeling special, observed or chosen as a research participant. The qualitative data helped to elucidate this fact, therefore highlighting the benefit of a mixed methods study design for the evaluation of complex interventions (439).

Incidental benefit due to time spent with participants

The staff team at the study site see approximately 400 patients per day, and depending on the presenting complaint, clinical appointments are about 5 minutes long. The control study arm received five of these appointments over the four month study period. The intervention group received a minimum of seven appointments, each lasting from 45 minutes to an hour of one on one time with an experienced HIV nurse trained in palliative care. This means that including data collection interviews, the intervention group received a minimum of 540 minutes or 9 hours of contact time, whilst the control group received about 250 minutes or just over 4 hours.

When studying the mental health and well-being of a known stigmatised group it is reasonable to assume that the group, who received a minimum of nine hours of contact time over four months, would respond more positively than a group who received about 4 hours, of which 25 minutes were with a health care professional, over four months. Participation in the study, and responding to the questions in the outcome measures was meant to be simply a data collection exercise. However in a stigmatised and socially isolated population, interaction with a friendly, accepting, non-judgemental, professional researcher has therapeutic impact, as seen in the findings of the therapeutic aspects of participation.

This highlights that there were in fact three levels of participants of interest to this study: the intervention participants who received the intervention and 5 interviews with a researcher, the control participants who received standard care and 5 interviews with a researcher, and the participants at the clinic who received standard care and whose outcomes we could not measure without most likely affecting them. Indeed an interesting and important question is the extent to which it is possible to measure mental health and well-being outcomes in a socially isolated and stigmatised, minimally literate population, without introducing bias. Potentially, non-participant observation of clinical encounters could be used to explore this group, without affecting their outcomes through social interaction. This approach may help to gain insight into this unstudied group

Systematic bias

Recall bias affects all studies which rely on participant memory and retrospective data collection methods. The extent of recall bias is affected by the type of knowledge, its importance to the participant and the time elapsed since the event (440). Recall bias was mitigated in this study by limiting the time between study exit and qualitative interview. Recall bias is also associated with social desirability, with data more likely to be recalled by participants if it is socially desirable.

Social desirability bias can be separated into two components: self deprecation and other appreciation (441). This bias reflects the respondent's tendency to deny socially undesirable traits and emphasise more desirable traits, particularly from the imagined perspective of those whom they respect or wish to impress. Participants in this study reported that they were concerned about how the study team viewed them, primarily because they liked their company. One participant expressly described how she felt she should report benefit, even if she did not experience it, because she did not want the researchers and study nurses to become discouraged by her lack of progress. It is possible that others acted similarly.

The researcher collecting the qualitative interview data was seen by participants as part of a team which provided the care. Should the respondent want to please the interviewer, who was seen as an educated but approachable person, and potentially the person responsible for bringing palliative care to the clinic, they may well have spoken about their experience in a more positive light. To counteract this possibility, participants were told that the interviewer was interested in their experiences and that there was no right or wrong answer to the questions she was asking. She was also trained to minimise social desirability, by maintaining a neutral stance and approach to participants, and not asking leading questions during qualitative interviews. Social desirability could have been further mitigated by having a different researcher collect the quantitative and qualitative

data, thus reducing the connection with the intervention and trial. This was not possible due to financial and logistical constraints.

Interviewer bias, where the data collected is affected by the interviewer, may also be a concern for this study, however this was reduced in recruiting the interviewer due to her experience in the field, and extending her training in interview technique, including how to minimise systemic bias in health systems research (440). Interviewer bias may still have affected the data collected, as previously discussed, even an open and non judgmental affect can have an effect on the participants if they are not used to openness and not being judged.

In this study, participants participating in the qualitative interviews were interviewed at the location they received the intervention or where they completed the research questionnaires. It is likely that the data will have been affected by recall bias, particularly those for whom the study was uneventful or those for whom there was a bigger time delay between exiting the trial and participating in the interview. This might have been mitigated further, by reducing the time between trial exit and qualitative interview.

7.5.4. Ethical Considerations

7.5.4.1. Palliative care delivered by outpatients clinic nurses

Informal communication with the nursing team indicates that the study nurses had difficulty maintaining emotional distance from the participants to whom they were delivering palliative care. Previously in their careers, there had been no time in a clinic encounter to interact meaningfully with their patients, and therefore they had never listened to patient concerns and difficulties in any depth, and had never before experienced the intimacy this created. They reported difficulties managing their personal feelings as a result, and described grieving for participants who died during the trial in a way they had never before, feeling deep sorrow and relying on each other for support.

During the palliative care training which the study nurses received in preparation for delivering the intervention, personal care was taught and discussed, acknowledging the difficulties associated with increased exposure to human distress, suffering and death. In addition, the nurses had support from an experienced palliative care professional who guided them through the personal and professional challenge of delivering palliative care for the first time. It appears that this training and support was insufficient to prepare the nurses to healthily manage the emotional labour of caring for participants with severe emotional pain.

While it is normal and human for nurses to feel sadness at the death of a patient, the extent to which these nurses described their grieving was concerning, particularly with the longer term view of widening access to supportive or palliative care to all HIV positive patients. When palliative care is delivered in established centres, a wider community of practitioners is immediately available for the novice to learn from and be guided by. The experience of the nurses in this study suggests that increased support should be made available, in addition to more time preparing staff for the death of patients who will become known to them.

However, it is also important to note that despite this difficulty, the nurses also reported feeling much more fulfilled by their role as palliative care nurses during the study. They felt rewarded by the relationships they made through which they saw the participants improve, due in part to their efforts.

7.5.4.2. Care beyond the study period

Unlike other trials of palliative care interventions, patients who exited this trial were expected to continue to live with their condition for many years. This meant that the needs which were identified and addressed by the intervention would no longer be addressed once they returned to standard care, and may remain unaddressed for many years.

This was problematic for eight participants recruited to receive the intervention care package, who continued to require a higher level of analgesia than was available at the standard care clinic after trial exit. To address this, the research team worked with the local hospice to source the appropriate medications to these patients for a maximum of two months, by which time the symptoms had resolved. Regardless, the patients are now aware that there is another way of addressing their medical treatment and care needs, namely palliative or holistic care, which could create distress if they felt the standard care was inadequate.

7.5.4.3. Financial reimbursement

Participants reported gratitude for the financial reimbursement they received, ostensibly for travel expenses. However, they reported using the money for purchasing higher quality food, medicine and health tonics and supporting their family financially. This raises two issues.

First, participants allocated to standard care therefore may have purchased medicines and tonics, which were inaccessible to patients in standard care who were not participating in the study. Whilst this does not strictly fit the definition of trial contamination, if these medicines and tonics were

effective, the comparative treatment effect of the intervention may be reduced, and the possibility of a type II error increased (442).

Second, financial reimbursement appears to have affected participants' mental health and well-being. Essentially, reimbursement was identified as a therapeutic aspect of participation, which was not its primary purpose (replacing travel expenses). This therapeutic effect was likely due to the fact that the amounts distributed were considerably more than needed to cover their travel.

Participants received a flat rate, regardless of distance travelled. This approach is recommended by national research councils (425), but has also been criticised for being usually excessive, inappropriate, unaffordable to those unfunded by industry sponsors and ultimately unfair to participants who are paid the same amount but who incur different costs, depending on the distance travelled (443). Our participants received 400 Kenyan Shillings. Minimum daily wage for an unskilled employee outside of Nairobi or other major cities in Kenya was 264.50 Kenyan shillings in 2013 (403.80 for semi-skilled or assistant role, 562.96 for skilled such as baker or general clerk) (189). The TOPCare study offered almost the equivalent of a day and a half's wages to reimburse participants for their transport costs. This seems excessive, and yet was recommended by local stakeholders and cleared by the Kenyan and London based ethics committees.

It is universally recognised in trial communities that giving participants money to reimburse for transport is not the zero sum transaction described in research protocols, but a transfer of net value to the study participant (416, 444). This transfer usually occurs in a context where, in comparison to the research institution, the individuals participating in the research are extremely poor (425). Molyneux et al. conducted a study to support the development of guidelines for benefits and payments for research participants, and found that whilst it is generally agreed that benefits and payments should ensure that participants should be compensated for expenses, excessive payments or incentives distort the decision making processes, as those in poverty may participate against their better judgement (425). In addition, they highlighted cases where women had returned home with their transport money given by the research facility, which had disrupted gender roles within the household and led to conflict (425). Molyneux et al. recommend that payments be set based on distance between the research facility and residential zone, and should include a small amount to compensate for a drink or snack for the journey (425). This approach, whilst introducing a layer of complexity to transport reimbursements, would reduce the therapeutic effect of this extra money and clarify the effect of the intervention. Currently we cannot be sure how much of the therapeutic effect seen is due to the alleviation of financial constraint.

A further potential problem from this excessive reimbursement of travel expenses is that it could potentially have acted as an inducement for participants to consent. Should it have become common knowledge within the clinic that reporting pain or symptoms meant inclusion in the study, which guaranteed small but regular source of income for the next five months, this could have influenced decision to participate, or even encouraged participants to falsify symptoms to ensure recruitment. To prevent this effect, at recruitment, participants were only told of the amount they would be reimbursed after completing the baseline interview. In addition, the refusal rate of 56% would suggest that this effect was not significant.

It is difficult to address this issue, without addressing the issues of the wider context of the trial (poverty, social deprivation), and it is morally difficult to stipulate that people who have financial difficulty should not be helped in case this decreases the effect of the intervention.

7.5.4.4. Informed consent

Participants in research are vulnerable to potential exploitation, particularly when experiencing pre-existing vulnerabilities such as illiteracy, sickness or poverty (445, 446). A lack of appreciation of the differences in culture and life experience and disparities in wealth has been a barrier to understanding the ethical dilemmas of research conducted in LMIC by privileged researchers from more HIC (445). Informed consent is essential to preserve the dignity, safety, privacy and human rights of research participants, and remains an important but complex issue in cross cultural research (445)

The study team was clear that an ethical approach to consent was essential. Actions taken include providing prospective participants with culturally and language appropriate consent materials and a Kiswahili speaker to discuss the risks and benefits in detail.

In the context of this study, many reasons were given for consenting to participate in response to questioning during the phase 2 qualitative interviewing. Many participants reported that they had high levels of unmet informational need, which they hoped to address through study participation. They also reported that they had unresolved symptoms and pain, which influenced their decision to participate. Whilst they were well informed of the study content and requirements, their ability to make a decision may have been unfairly influenced by this unmet need.

Informed consent is a very difficult aspect of a study. As suggested previously, providing increased information, which would be the preferred route in HIC, could be confusing for people with different

cultural and educational backgrounds. On reflection it is my opinion that in the informed consent procedure adopted in this study was as high quality as was possible.

7.6. Future work

7.6.1. Clinical contributions

The study findings are discussed below, in the context of improving the clinical care.

7.6.1.1. Palliative care for PLWH in Kenya

Baseline data from this study identified unmet psychosocial and spiritual need at recruitment, indicating that the holistic needs in patients with life limiting conditions in the clinic study site are not being met. This could be a result of the medical focus of the undergraduate nurse training curriculum for nurses attending the University of Nairobi described previously (194), or a general lack of prioritisation of psychosocial needs due to the dominant biomedical discourse among staff and the necessary rationalisation of staff time due to the volume of patients (see Section 1.4.1.1, Pg 45). This would be compatible with findings from a study by Gott et al, that the dominance of the biomedical discourse and its associated focus on 'cure' as the only legitimate approach to care is a barrier to the delivery of holistic palliative care at any time but the terminal phase of life (447).

In an organisation where this philosophy of cure as the only legitimate form of care is strongest, it is likely that the perspectives of professionals from primary health (448) and nursing (199), with a more established record of holistic multidimensional approaches to care, are less well received. In these environments, palliative care as a medical speciality which has moved beyond the biomedical domain, to a less cure-focused, more patient-centred view has much to contribute to patient well-being (449).

The implementation of a short training package in palliative care for the clinic staff may help staff recognise the importance of attending to patients' psychosocial problems, and how this contributes to holistic well-being in PLWH.

7.6.1.2. Peer educators as treatment navigators

Participants reported both that they had difficulty articulating their problems in the standard care clinic, and an appreciation of being treated with compassion and being known by the study team. Peer educators could meet these needs relatively inexpensively.

Peer educators do currently exist in the standard care clinic, but their role is limited to health education provision for a small number of patients. Their role should be extended to support patients as a 'treatment navigator' and to monitor patient progress and well-being. They could meet with the patient before they met with a healthcare professional to discuss their holistic well-being. This would serve as a space or forum to discuss their experiences of HIV (167), and also fulfil the needs of being known, listened to, talk to relieve burdens, and to engage in open communication. With some training, peer educators could use a PROM such as the APOS as a springboard for discussion, and to assess the patients quickly and efficiently to identify areas of potential need. They could monitor and track previous problems and support the patient in accessing necessary support, and in preparing patients' questions for a clinical encounter with a nurse or medical officer. This would assist the patients in articulating their problems, to make sure they were resolved. Following our findings regarding the benefits of a non-judgemental approach, the peer educators should also be trained in patient empowerment methods, and in being non-judgemental and maintaining patient confidentiality. This position would not need much training, but should be paid to denote the importance of the role.

Potential patients who might benefit from these services could be identified by the nursing staff, to whom most of the patients are familiar, but ideally patients could also self-refer to the peer educators to ensure that all who felt they needed help could access it. This intervention would encourage patients to take care of their holistic well-being needs and not simply manage the physical aspects of HIV. This would entail a shift in clinic culture which would require support from those in senior management.

The proposed peer educator intervention could be simply evaluated through simple cross sectional study, screening multidimensional wellbeing in a random sample of the clinic population not accessing the peer support/trackers, and comparing it to those who were receiving the supportive service.

7.6.1.1. Use of traditional healers

When participants described having time to talk about their problems, some compared it to visiting a herbalist, or traditional healer. This is common in SSA, where most people visit traditional healers in parallel with biomedical practitioners (450), where the perceived role of the physician is to relieve symptoms, and the traditional healer to explain the cause (451).

Traditional healers outnumber biomedical practitioners in most countries in SSA, particularly in rural areas, and therefore represent an accessible and knowledgeable community resource (451, 452).

They routinely provide informal patient-centred care, which is culturally accepted and delivered in the context of their understanding of indigenous knowledge systems and models of helping (450, 452, 453).

Traditional healers should be explicitly and openly integrated into healthcare provision as community contact points. They could provide a listening service to PLWH, to help them articulate their problems, and referring directly to the clinic when beyond their level of expertise. Mutual respect between traditional and biomedical practitioners, lacking in many previous programmes, should be a priority for programme managers to ensure optimal benefit from both approaches (450).

7.6.1.2. Material support in the context of poverty

Although in our study, the financial reimbursement of travel expenses was intended to be a zero sum transfer, to reduce barriers to participation in the trial, the amount given was excessive and created surplus to be used to alleviate distress associated with financial constraint, after travel was reimbursed. It effectively became part of the intervention, albeit received by all participants and not only those allocated to the intervention arm. This is unsurprising, as financial constraint is recognised as a determinant of mental health and wellbeing in the literature, as discussed in section 1.2.2.3 (56). Participants in sample were relatively poor, as demonstrated in Table 5-6, (4% owned a car, 21% owned a bicycle and 25% owned a fridge). This highlights difficulty of conducting research in a non-exploitative way in the context of poverty. In addition for palliative care, if care is to be holistic, potentially interventions which improve participant's socio-economic status, should be considered.

Recent evidence suggests that the provision of food security and food assistance can have a positive impact on treatment adherence for PLWH, who are co-infected with TB (454). It is possible that in this study, as in ours, the provision of material support relieved financial constraint and the associated mental health distress, and enabled participants to engage in their health and well-being.

These findings should inform future interventions and research in this population, and researchers should bear in mind the therapeutic impact of relieving financial constraint as an additional source of benefit to their intervention. An evaluation of the effectiveness of an economic intervention would be pertinent to our findings that relief of material suffering improved psychological well-being, and would reflect the wider literature on the social and environmental determinants of health and well-being (73, 79, 415).

7.6.1.3. **Medication**

Our study has identified the unmet need for mild to strong opiates for pain control in this sample of PLWH. It is therefore essential that adequate pain relief be made consistently available, both in terms of an improved supply chain to prevent stock-outs in Kenya, and in terms of financial accessibility.

A recommendation from this study is that clinical staff in HIV settings are trained in the use of the WHO pain ladder, which is simple to use and recommends inexpensive medication to control pain (385). This should improve care provided the pharmacy is stocked accordingly. Training should also be provided to hospital staff responsible for the supply chain of essential medicines to prevent stock outs. This is not an expensive addition to current care, but merely optimisation of existing structures, which is particularly important when making recommendations for changes in healthcare in LMIC.

7.6.1.4. **Compassionate care**

Our findings indicate that compassionate care is not widely practiced in the standard care clinic, probably largely due to the heavy patient load and lack of time. In light of our findings on the impact of a compassionate approach on patients, and the wider literature on the subject, this should be addressed as a matter of urgency by the senior management of the clinic. It would entail a shift in culture, increasing the priority and routine of delivering care with a compassionate approach, and would require staff training to promote compassionate, patient focused care encounters. As this sometimes can take more time, structural reorganisation may be necessary for nurses to enable patients to be listened to, and an opportunity to feel respected and treated with dignity.

The structural reorganisation would require commitment and continuing support for clinic staff from senior management, to ensure that changes made were implemented. It could be evaluated using routine data collected from the clinic such as ART adherence rates, attendance rates, and loss to clinic follow-up in the community. In addition patient's satisfaction with care could be assessed using a simple indicator on leaving the clinic. Due to low levels of literacy, this could be achieved by placing a token or slip of paper in one of three boxes: satisfied, ambivalent or dissatisfied with care received in the clinic today. Should there be many patients reporting dissatisfaction, this could be explored through qualitative interviewing.

The use of a measure of patient rated clinician compassion or empathy such as the Jefferson Scale of Physician Empathy (JSPE) (455) or the CARE measure (456) could be used considered and if found

favourable, employed at regular intervals. Although it is recognised that empathy and compassion are not synonymous, our study participants perceived expressions of empathy as compassionate, and therefore evidence from patient rated empathetic consultations would be informative for practice development in the absence of a tool to rate compassion.

7.6.1.5. Routine screening and one off holistic care encounter

The study found benefits to intervention participants compared to those receiving standard care after one month, possibly due to the initial high intensity of palliative care appointments in the initial weeks of the study (Table 3-2). As a result, screening and a one-off holistic care appointment may be effective for improving holistic well-being of patients attending the clinic. A screening tool, such as the APOS, could be used to assess for multidimensional needs of patients attending the clinic, with referral to a holistic service for those reporting distress, where time could be taken and a holistic assessment of well-being performed.

To evaluate this intervention, a similar approach to the TOPCare trial design could be used. A random sample of patients should be screened, and if problems were identified in any dimension, participants should be randomised to receive either a brief one off palliative care encounter or standard care. All patients would be screened again after a few months to evaluate the effectiveness of this intervention. Short term palliative care interventions such as this have been trialled in patients with multiple sclerosis, and found to reduce symptoms and caregiver burden (457).

7.6.1.6. PROMs as a prompt in practice

The importance of the PROMs as a prompt for participants, particularly those not receiving the intervention could be another potential area for an intervention. Patients waiting in the clinic to be seen by the nurse or medical officer should use the time to complete a simple PROM, such as the APOS as a short, concise holistic assessment tool.

This could serve as a prompt to remind the patient to address problems when they are seen by the nurse or medical officer, and also as a simple data collection exercise. If resources were available, patients could complete these using an electronic device, which could read the questions to them through a headset, to avoid problems with low literacy. They would record their response using the touch screen, which would be stored as routine data, used to track patient progress and improve the clinical care. Patients could request print outs of their progress to act as a further prompt for self-reflection and self-care.

To trial the effectiveness of this simple intervention on patient outcomes, other routinely collected data such as CD4 count or adherence data could be compared for those randomly allocated to complete the PROMs with those not. This would allow the evaluation of the effect of completing the PROMs separate from the effect of the social interaction with the researcher described during this study.

7.6.2. Implications for policy

Findings from this study provide evidence that should be integrated into HIV care guidelines, for the promotion of holistic well-being for PLWH.

All patients should be screened for multidimensional needs at regular intervals. This, with appropriate referrals and treatment, will prevent early signs of mental distress developing into severe mental illness, which will have an impact on treatment adherence and the future success of ART in controlling the HIV pandemic (19).

Health education should be increased, and provided at all times and in diverse ways which are appropriate for the range of patients, adapted to their level of literacy, anxiety and time availability. It should be delivered only after time has been spent listening to patients, to ensure that the information provided is timely and appropriate, and should be delivered in a context of trust, which will increase information retention and the likelihood of a positive outcome.

Appropriate analgesia should be available and accessible for patients at all times in the clinic pharmacy. Steps should be taken to prevent stock-outs of analgesia included on the WHO pain ladder, which is an effective and inexpensive approach to pain management (385).

Patients should have access to specific social support networks for PLWH as a forum to discuss their experience of HIV in a non-judgemental environment, free from the effects of stigma. Our findings indicate the importance of social and emotional support and the potential to learn from others in the same situation. The stigmatising nature of HIV means that a safe and non-judgemental forum to discuss their experiences is rarely available, and evidence suggests that this could benefit patients in terms of health education and social and emotional support (167).

Material support should be made more available, consist of more than simply financial reimbursement, and be more responsive to the local context and need. This would mitigate the additional constraints placed upon a family with a member living with HIV/AIDS, particularly if the affected member is the main breadwinner, and could contribute towards the extra costs incurred through illness, such as medication not covered by basic clinic care. It would also alleviate

psychological distress. Creative income generating programmes should be explored for this patient population, to mitigate the effects of sickness due to HIV on family life. This may involve collaborations with community-based organisations in the area, working in areas such as microfinance, rolling loans or projects that increase skills and employment options for PLWH.

Senior hospital management should provide leadership and support for clinicians to develop a more patient centred, respectful, caring and non-judgemental approach to care. This may involve increasing staff numbers to reduce workload, stress and burnout, role modelling a compassionate approach to patient care and improving team-work in clinics. Clinical supervision or peer debriefing would also recognise and mitigate any negative effects of the emotional labour of this approach to nursing. This would increase staff and patient quality of life, mental health and well-being, and patient reported satisfaction with care.

7.6.3. Academic and theoretical contribution

7.6.3.1. Stigma

HIV associated stigma is a major barrier to the success of the international effort to curb the spread of HIV, and thus the eradication of stigma is recognised as an important goal for international donors and other bodies working in the field of HIV (10, 16, 18, 458). The findings in this study, and the novel mapping of findings regarding stigma and stigma resistance onto a pre-existing theoretical model of shame resistance, demonstrate the importance of further developing and testing a theoretical framework of shame resistance theory among stigmatised PLWH.

There is evidence that interventions designed to enhance self compassion, in which participants explore the concepts of self-criticism and self-compassion in a group context, can enhance resistance to HIV-associated stigma (459). One study found that a group therapy intervention resulted in significant reductions in anxiety, depression, feelings of inadequacy, self criticism, self persecution, hatred of self, social comparisons, seeing others as “shamers” and submissive behaviour and significant increases in self reassurance and self compassion (459). This appears to follow the shame reduction theory described by Van Vliet, in which those who are shamed reframe their experience, and begin to separate themselves from the shaming experience, and in the process recover (421).

Self-compassion and shame resistance interventions should be further developed and evaluated in terms of their impact on the experience of stigma and the ability of people with HIV to resist stigma and shame. If the proposed mechanism for the reduction of HIV associated stigma is verified and sustained, the implications for PLWH, both in terms of public health and individual health, are

considerable. People at risk and those who suspect they may be positive, would test earlier, and more frequently. This would lead to those eligible accessing treatment earlier, which would lead to a reduction in infectiousness, and could prevent transmission to other uninfected people. Retention in care would be easier as patients would not fear being seen at the clinic and inadvertently disclosing their status. Patients would freely disclose their status and therefore access the emotional and tangible social support they need to cope with sickness.

7.6.3.2. Refining the wider trial study design

The primary outcome of the TOPCare trial was reported pain. The secondary outcome of the trial and the primary outcome of this thesis was psychological quality of life.

To study the effect of an intervention on mental health and well-being, particularly in socially isolated populations, the trial design must minimise the effect of increased social interaction beyond receipt of the intervention. If this is not adjusted for in the study design, as we have found, it is difficult to separate out the effect of the intervention from the effect of social interaction through participation in the study.

One possible solution could be to identify the control and intervention arm patients and begin collecting repeated measurements of observational data on their holistic well-being before initiating an intervention. This would allow for any changes due to study participation increasing social contact to be measured in both study arms. After one month, the intervention and trial could be initiated and therefore any intervention effect more clearly identified.

7.6.3.3. Ability to share and educational attainment

The findings show an association between increased ability to share and decreased educational attainment. This finding conflicts with the wider literature on social support and education, and as such warrants further investigation in this population.

7.6.4. Methodological contributions

This study demonstrates the use of mixed methods to evaluate a nurse-led intervention for PLWH in SSA. To the best knowledge of the study team, this is the first study to evaluate a palliative care intervention integrating findings from both quantitative and qualitative methodological approaches on a HIV positive sample. The use of mixed methods enabled exploration not only the outcomes of the intervention, but also the processes and mechanisms by which these outcomes arose. In

identifying the processes, and in essence, what was effective and why, the intervention can be more easily adapted and replicated for different clinical contexts and patient populations.

Five quantitative data analysis techniques were used to analyse the quantitative data: linear regression, ordered logistic regression, logistic regression, area under the curve and multi-level modelling. Each technique has its own advantages and disadvantages, and contributed to addressing the study objectives. As the data were highly non-parametric, ordered logistic regression was used when assumptions were not violated. Use of non-parametric statistics is relatively rare in the published data, even when data are subjective measures and collected using an ordinal scale. This approach produces a more conservative result, thus maintaining the integrity of the study and increasing the likelihood that any associations identified are not the result of statistical error.

Monthly time point analysis generated comparison data, enabling between arm comparisons at each time point, and the identification of the effect of palliative care after one month of intensive support.

The use of multi-level modelling of ordinal variables has not been previously used on APOS data and therefore is a novel contribution of this thesis to the research field. It enabled the analysis of repeated measures, adjusting for the bias which would be created by correlation of data by patient. In creating a longitudinal summary measure through the use of AUC, analysis of association between longitudinal change and clinical and demographic variables was possible.

In addition this study provides a detailed description of the content of a patient-centred palliative care encounter for PLWH, for each appointment, based on patient need. Palliative care for PLWH is relatively under-researched within the wider palliative care research context, and as such this data was never before been collected and reported in such detail. In addition, this highlights the contribution of palliative care for PLWH, and identifies components that could be added to standard clinic care to improve holistic outcomes.

The findings also highlight that the traditional view of the researcher as independent observer is flawed. The identification of PROMs as prompts to self-care leading to improvements in mental health and well-being demonstrate these difficulties and perhaps the impossibility of collecting outcome data from a complex intervention without influencing the outcome. In addition the impact of context on outcome is described through the participants' reports of the importance of material support in the process of therapeutic benefit, thus highlighting the value of acknowledging the open system in which the intervention was delivered (244, 263).

The use of mixed methods is recommended for the development and evaluation of complex intervention such as palliative care (27). In this case it enabled a detailed examination of the experience of receiving a palliative care intervention, and an exploration of the associations observed in the quantitative outcome measures, through integration and thus expansion in the qualitative data, in addition to exploration of active ingredients and their causal mechanism. This integration of methods creates a richer understanding of the participant experience and adds to the work of Plano-Clark, O’Caithain and Curry, who advocate for the use of mixed methods evaluation in health services research (242), particularly as in this case, interpretive qualitative methods within an RCT (264).

Following this, the study also highlights and attempts to resolve the ontological tension underlying the use of a traditional RCT design in identifying complex causation (244, 261). If evaluation of the effectiveness of the intervention were based solely on the quantitative data analysis, we would be unaware of the contribution of compassion, social support, communication PROMs as prompts and material support to the outcomes observed. The use of critical realist theory as a philosophical basis to resolve the ontological tension inherent in mixed methods research is also a relatively novel contribution. It has much to offer the science of evaluation research in palliative care, openly acknowledging that outcomes of social interaction are complex, context dependent, and usually have multiple causal mechanisms, of which we can identify only some (244, 261). This approach describes reality as composed of the empirical, real and actual domains (see section 3.3.2.2), which opens the debate to the possibility of exploring how causal mechanisms operate to bring about change.

Conclusions

This study found that a nurse-led palliative care intervention for PLWH on ART was effective compared with standard care in improving psychological quality of life, the ability of participants to share their feelings and in reducing psychiatric morbidity, but had no effect on levels of worry. Barriers to therapeutic benefit were persistent physical, social or financial problems. The active ingredients of the intervention were identified as health education and counselling, medication, and providing time to talk to enable participants to articulate their problems.

These findings suggest that simple additions of health education, access to medication and allocating time to talk and articulate problems could be sufficient to address many of the mental health and well-being problems experienced by PLWH. These interventions could be achieved economically, through minimal staff training and optimising pre-existing supply chains for medication. Time for participants to talk could be created through extending the role of peer educators, or integrating the expertise of traditional healers into the care delivered.

Participation in the study was therapeutic beyond receipt of the intervention. Participants in both study arms described benefit from experiencing compassion, social support, communication and material support and through using the PROMs as a prompt to self care. These therapeutic aspects of study participation were effective through establishment of a trusting relationship, first between the study team and the participants, and then amongst the community, and through increases in feelings of personal control and thus self esteem and self-image.

These therapeutic aspects of participation highlight the current low level of trusting relationships and social support described by PLWH, possibly due to HIV-associated stigma. This study found that trusting relationships led to a rebuilding of self-image, the forging of stigma resistant identities and improvements in mental health and well-being. A theoretical contribution of this study was to map this rebuilding process onto pre-existing theories of shame resistance, extending the theory to HIV-associated stigma. Should a model of care based on this theory of resistance to stigma be proven effective, the implications for PLWH could be significant, as it would improve access to HIV testing, treatment, medication adherence and the social emotional and physical well-being of PLWH.

This study also made four methodological contributions. First, the study demonstrates the value of mixed methods in the context of an RCT, which although generally recommended, is still relatively novel in palliative care research. Each methodological approach contributed to a sophisticated understanding of the complex intervention, and the influence of contextual factors on its implementation and effectiveness. Secondly, the paradigm of critical realism was found to be a

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useful stance from with to conduct mixed method research, resolving the ontological tension, and contributing an emphasis on contextual factors and underlying causal mechanisms, which helped to identify and conceptually integrate the findings. Thirdly, the use of multilevel modelling to analyse repeated measures has never before been used on APOS data. This analysis can be done effectively to adjust for the potential bias created by correlation of repeated observations by patient, and should be used in future research, to generate more rigorous findings using the APOS data. Fourthly, this study has deepened understanding of the methodological complexities of conducting an RCT in context of social need, such as poverty and social isolation due to stigma.

This study has shown that a nurse-led palliative care intervention is an effective model of care for meeting the holistic needs of PLWH on ART, describing the effect of health education, medication and time to articulate problems, intrinsic to the palliative care approach. The participants' appreciation of compassionate care, social support, communication, prompts to self-care and material support highlights the difficulties of conducting research in a population with complex needs, related to poverty, stigma and social isolation.

The findings of this study represent a novel contribution to the evidence base for the development and evaluation of a holistic model of care, which helps to meet the multidimensional needs of PLWH experiencing HIV infection as a chronic condition, particularly within the constraints of healthcare systems in LMIC. Furthermore, the findings of this study support efforts to increase resistance of PLWH to stigma and discrimination, with associated benefits for public health as well as individuals' quality of life.

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Appendices

Appendix 1 – Timeline of PhD and TOPCare study

Date	TOPCare trial event	My timeline
09/2010	Study designed Funding grant submitted	
10/2010	Funding granted Ethics approval submitted	
11/2010		
12/2010	Ethics approval granted from Kings and KEMRI in Kenya	
01/2011	Study nurses appointed and trained	
02/2011	Study documents developed and standardised operating procedures finalised	
03/2011	Ethics approval granted from South Africa Study launch in Cape Town South Africa Training researchers	Started PhD Finalise TOPCare study documents
04/2011	Recruitment starts in Kenya	Monitoring recruitment
05/2011		
06/2011		
07/2011	Recruitment in Kenya stops and recommences	Visit to Mombasa to resolve matters arising during recruitment
08/2011		
09/2011		Design qualitative component of study
10/2011		
11/2011		Apply for ethical approval for qualitative data collection
12/2011		
01/2012	Apply for extension of trial period to Kenyan and Kings ethics submitted	
02/2012	Recruitment and data collection starts in parallel South African study site	
03/2012	Approval for extension of study period granted	Kings ethics approval for qualitative data collection granted
04/2012		
05/2012		Kenyan ethics approval for qualitative data collection granted
06/2012	Qualitative data collection begins in Kenya	

Appendix 1 – Time line of PhD and TOPCare study

07/2012	Quantitative data collection complete	PhD upgrade successfully completed Recruitment for transcription and translation of qualitative data begins
08/2012		
09/2012	TOPCare study protocol paper submitted to BMC Infectious diseases	Analysis of quantitative data commences
10/2012	Qualitative data collection complete	
11/2012	TOPCare study protocol published in BMC infectious diseases	Translation of qualitative data complete Analysis of qualitative data commences
12/2012	Dissemination of preliminary findings to patients and staff in South Africa and Kenya	
01/2013		
02/2013		
03/2013		
04/2013		
05/2013		European Association Palliative Care Conference – poster presentations
06/2013		Systematic review submitted to International Journal of Nursing Studies
07/2013		
08/2013		
09/2013		AIDS Impact conference – oral presentation
10/2013		
11/2013		
12/2013	Recruitment data paper submitted to BMC research Notes	
01/2014		
02/2014		Systematic review published online in the International Journal of Nursing Studies
03/2014		
04/2014		RCN International Research Conference – oral presentation
05/2014		
06/2014		
07/2014		Submit PhD

Appendix 2 - Checklist for 2 weekly site phone call

Report over past 2 weeks

1. How have things been going?	
2. Have you met any problems?	
3. How many days were you recruiting for?	
4. Report for last 2 weeks. Number of patients screened by triage nurse. Number scoring 3-5 on pain/symptoms. Number assessed against exclusion criteria Number invited into study Number refused Number new enrolled Number randomised to intervention Total enrolled from start Total number completed	
5. Triage nurses Did they have any problems? Did they report number screened?	
6. Data Entry Has data been entered for all these patients? Have you made a backup?	
7. Plans for the next month. How many days a week do you plan to recruit? How many patients do you plan to recruit in the next month?	

Appendix 3 – Systematic review paper

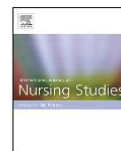
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Review

Experience of persistent psychological symptoms and perceived stigma among people with HIV on antiretroviral therapy (ART): A systematic review



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ABSTRACT

Background: Advances in HIV care have resulted in increasing numbers of HIV patients receiving antiretroviral therapy and achieving viral control. This has led to a focus on the biomedical aspects of care, leaving the data on psychological and social problems relatively neglected; in fact they have never before been systematically reviewed. If present and unmanaged, psychological and social problems are associated with unnecessary suffering and non-adherence to medication, with potentially serious clinical and public health consequences.

Objective: To assess the prevalence of depression and anxiety reported in the literature, and the presence or absence of the experience of stigma among HIV positive people on antiretroviral therapy.

Design and review methods: A systematic review in line with PRISMA guidelines. The prevalence data from retained studies were analysed by study location and data quality. **Data sources:** Five databases were systematically searched (Embase, PsychINFO, MEDLINE and British Nursing index and Web of Science) from 1996 (first availability of highly effective antiretroviral therapy) to August 2013 using a predefined search strategy.

Results: Sixty-six original studies identified the prevalence of depression, anxiety and presence or absence of the experience of stigma. The mean point prevalence of depression was 33.60% (SD 19.47) with lower reported point prevalence in high income countries (25.81% (15.21)) compared to low and middle income countries (41.36% (21.42)). The one-to-four-week period prevalence of depression was 39.79% (21.52), similar in high income countries and low and middle income countries. The point prevalence of anxiety was 28.38% (17.07), with a higher prevalence in low and middle income countries (33.92% (10.64)) compared with high income countries (21.53% (22.91)) with wide variability. The mean point prevalence of stigma was 53.97% (22.06) and 1 year period prevalence 52.11% (25.57). Heterogeneity in both sampling and methodology prevented meta-analysis of this data.

Conclusion: HIV positive patients on antiretroviral therapy report a higher prevalence of depression and anxiety than the general population, which nursing assessment and practice should address. Over half of HIV positive people report experiencing stigma. The difficulties with heterogeneous studies should be addressed through the development of a cross-culturally validated, multidimensional assessment tool in this population, and an increase in data disaggregated by risk groups.

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What is already known about the topic?

- Biomedical advances in HIV treatment have been significant in the past decade and access to treatment continues to improve internationally.
- Unmet psychological and social needs can have serious clinical and public health consequences: non-adherence, subsequent treatment failure and increased infectiousness.

What this paper adds

- The systematic review found that 34–42% of patients with HIV on ART experience depression and 21–40% of patients with HIV on ART experience anxiety.
- Prevalence rates of depression and anxiety are higher than in other chronic conditions and in the general population.
- Point prevalence of anxiety and depression are higher in low and middle income countries than in high income countries.
- 42–83% of HIV positive people on antiretroviral therapy report experiencing stigma or discrimination.

1. Introduction

The introduction and roll out of antiretroviral therapy has dramatically reduced mortality for people with HIV infection (UNAIDS, 2010a,b). In sub-Saharan Africa, following the introduction of antiretroviral therapy in the early 2000s, the number of annual HIV/AIDS-related deaths fell by 20% between 2004 and 2009 (UNAIDS, 2010a,b). Whilst this progress is commendable, a holistic approach to care requires knowledge of the extent of psychological symptoms and social problems of this growing population of HIV patients on antiretroviral therapy. This data has not yet been systematically reviewed in this patient population.

The World Health Organization (WHO) defines health holistically (“a state of complete physical, mental and social well-being” (WHO, 1948)), recognising that beyond the physical elements of well-being there are aspects of psychological well-being and social well-being which also contribute to health. Psychosocial and spiritual support is recognised by the WHO, UNAIDS and the President’s Emergency Plan for AIDS Relief (PEPFAR) to be essential to comprehensive HIV care (PEPFAR, 2006; UNAIDS, 2000; WHO, 2012a,b).

Living with HIV is associated with a burden of unmet psychological and social problems. Evidence from a UK study suggests that psychological distress is common among HIV positive gay men established on antiretroviral therapy (Harding et al., 2006). A systematic review of mental health problems in HIV patients in India of mixed treatment status (both on antiretroviral therapy and not) identified prevalence of clinician-rated depression, post-traumatic stress disorder, general distress and anxiety, substance abuse and general psychiatric morbidity above population norms (Das and Leibowitz, 2011). In Africa, a recent systematic review found 44–58% of all patients with HIV of mixed treatment status have psychological

problems, most commonly depression (Brandt, 2009). Furthermore, mental health problems are associated with poverty, unemployment and poor educational attainment (Brandt, 2009).

Unaddressed psychological and social problems have potentially severe clinical implications. A recent meta-analysis of international data identified a strong and consistent negative association between depression and adherence (Gonzalez et al., 2011a,b). This association between depression and low adherence presents a very real threat to the success of international progress in controlling the epidemic. For antiretroviral therapy to effectively control viral replication, patients must achieve optimal adherence (>95%), thereby avoiding resistance, treatment failure, increased infectiousness, morbidity and mortality (Bangsberg et al., 2000, 2001; Ruge et al., 2004).

Whilst regional and whole patient population reviews exist for depression, anxiety and experience of stigma in HIV patients, the international literature has not yet been systematically reviewed to examine the problems experienced by HIV positive patients established on antiretroviral therapy. This is a rapidly growing population due to the recent changes in antiretroviral therapy initiation guidelines, which now recommend antiretroviral therapy earlier in the disease trajectory (WHO, 2013). If the holistic needs of this population are not addressed, patients will be at increased risk of unnecessary suffering and poor adherence, resulting in increased viral replication, infectiousness, morbidity and mortality.

This review will enable practitioners to understand the scope of the problem and potentially identify patients for screening and subsequently appropriate support. It will enable policy makers to fit health care service provision policy to the needs of patients, and academics to conduct more informed, relevant research, including trials into the effectiveness of interventions to address these problems.

2. Methods**2.1. Review question**

A systematic review of the literature was conducted to answer the question “What is the prevalence of anxiety, depression and the experience of stigma in people with HIV infection on antiretroviral therapy?”

2.2. Definitions

For the purposes of this review, antiretroviral therapy was understood to be triple therapy antiretroviral treatment for the management of HIV infection (WHO, 2010). Anxiety was defined using the National Institute of Mental Health definition of anxiety as patient report of excessive irrational fear or dread (Health, 2013). Depression was defined using the WHO definition of unipolar depression as patient report of depressed mood, loss of interest or enjoyment and reduced energy (WHO, 2012a,b). Stigma was defined as an attribute behaviour or reputation which is socially discrediting (Goffman, 1963). Stigma is a common problem for people living with HIV/AIDS, often resulting in discrimination, which leads to or precipitates

problems with disclosure, social isolation and support (Deacon, 2006; Parker, 2012; Turan et al., 2011).

2.3. Design

A systematic literature review was performed in line with the PRISMA (Moher et al., 2009) statement and guidelines from the NHS Centre for Reviews and Dissemination (NHS, 1996).

2.3.1. Search strategy

Five databases were searched in August 2013: Embase, PsycINFO, Ovid MEDLINE, Web of Science and the British Nursing Index.

Within Web of Science the following categories were included: Public Environmental occupational health, Psychiatry, Infectious diseases, Health policy services, Psychology, Psychology multidisciplinary, Psychology social, Psychology applied, Psychology biological, Psychology developmental, Psychology clinical, Nursing, Paediatrics, Social sciences biomedical, Social sciences interdisciplinary, Social work, Social issues, Substance abuse and Tropical medicine.

Within Embase, Ovid MEDLINE, PsycINFO and the British Nursing Index, records between 1996 and 2013 week 34 were included. The search excluded papers not in English or French.

2.3.2. Search terms

Group 1: (targeting HIV positive patients): HIV, human immunodeficiency virus, AIDS, HIV/AIDS (combined using "OR"), Group 2: (targeting patients on antiretroviral therapy) antiretroviral therapy, highly active antiretroviral therapy, ART, ARV, HAART (combined using "OR").

Groups 1 and 2 were then combined using AND to make group 3.

Group 4: (Targeting patients experiencing anxiety depression or stigma): depression, sadness, anxiety, worry, stress, stigma (combined using "OR").

Groups three and group four were then combined using "AND".

To ensure maximum retrieval, all words were searched as a keyword, a subject heading and in the abstract or title. In addition to the database searches, reference lists of review articles were searched for relevant papers.

2.4. Inclusion and exclusion criteria

Inclusion and exclusion criteria are presented in Table 1. They were selected to identify the most relevant data regarding the range of prevalence of depression, anxiety and the experience of stigma in this population.

Each paper was evaluated by the first author against the inclusion and exclusion criteria listed above. Any paper for which inclusion was unclear was discussed with a second author (RH) and if necessary adjudicated by a third (IJH).

2.5. Data extraction

Common tables were used to extract author name, year of publication, country in which the study was conducted, study aim, study design, outcome measurement tools used, sample size and characteristics (age, sex and percentage on antiretroviral therapy), reported point or period prevalence of anxiety, depression and/or experience of stigma (mean, median and confidence intervals where available).

2.5.1. Analysis

It was anticipated that prevalence estimates would be biased by factors such as sample size, sample composition, tool selection (including potential use of unvalidated or unstandardised tools), socioeconomic context and the presence of co-morbidities. Each paper was critically appraised using the Loney data quality appraisal tool to identify these sources of bias (Loney et al., 1998). Data were synthesised by country income status: low and middle income status versus high income status as defined by the World Bank (WorldBank, 2012). The mean for the whole sample and for high income countries and low and middle income countries was presented, weighted by quality score, with more weight given to papers reporting studies of higher quality.

The epidemic is often described as generalised in low and middle income countries, meaning that is self-sustaining, transmission occurs through heterosexual sex and there is above 1% prevalence in pregnant women attending antenatal care (UNAIDS, 2011). Concentrated epidemics occur primarily in high income countries with populations at higher risk, which include as men who have

Table 1
Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
1. Study sample 100% HIV positive.	1. Editorials, opinion pieces, conference abstracts and reports of case studies.
2. $\geq 90\%$ of reported sample currently on antiretroviral therapy, unless data is disaggregated and reported separately by treatment status.	2. Papers not reporting prevalence of depression, anxiety or the experience of stigma.
3. Papers reporting prevalence of depression, anxiety or the experience of stigma in HIV infected persons on antiretroviral therapy.	3. Publications reporting studies with $\leq 90\%$ of HIV sample on antiretroviral therapy, if findings were not disaggregated by antiretroviral therapy status.
4. Publications reporting original studies of adults or children.	4. Publications of studies including patients only on prevention of mother to child transmission or post-exposure prophylaxis programmes (not antiretroviral therapy in response to patient disease progression).
	5. Papers not in either English or French.
	6. Papers before 1996, the advent of highly active antiretroviral therapy.

sex with men, previous or current users of intravenous drugs (IVDUs), and migrant workers. Because of a lack of detailed reporting by risk group, country income statuses served as a proxy for generalised or heterosexual sex-driven epidemics, or concentrated epidemics where those infected are more often men who have sex with men, previous or current IVDUs or migrant workers (UNAIDS, 2011).

2.5.2. Quality assessment

Paper quality was evaluated using the Loney quality appraisal tool, designed to appraise bias and reliability in papers reporting the prevalence or incidence of a health problem (Loney et al., 1998). The 8-item tool allocates a point based on the presence or absence of each criterion. The criteria are: random sampling, unbiased sampling frame, adequate sample size, standardised measures used, unbiased assessors, response rate >70% with description of refusals, reporting confidence intervals and subgroup analysis and description of study subjects. A maximum score of 8 indicates a high quality paper.

2.5.3. Reporting

First, study designs, outcome measurement tools and country of research were summarised. Second, prevalence data were presented by mean and weighted mean point prevalence and period prevalence data for all citations retained and by country income status in table and graphical form. If data were disaggregated by risk group, these were also reported to allow comparison of prevalence across difference patient groups infected by HIV. Weighted means were calculated using the data quality score as a weight, to give more weight to those studies with higher quality score.

3. Results

The search summary flowchart following PRISMA guidelines is presented in Fig. 1 (Moher et al., 2009). The characteristics of retained citations are presented in Table 2, with a Loney score of data quality (8 = best, 0 = worst).

A large proportion of citations were removed at the title screening stage of the review; however, this was

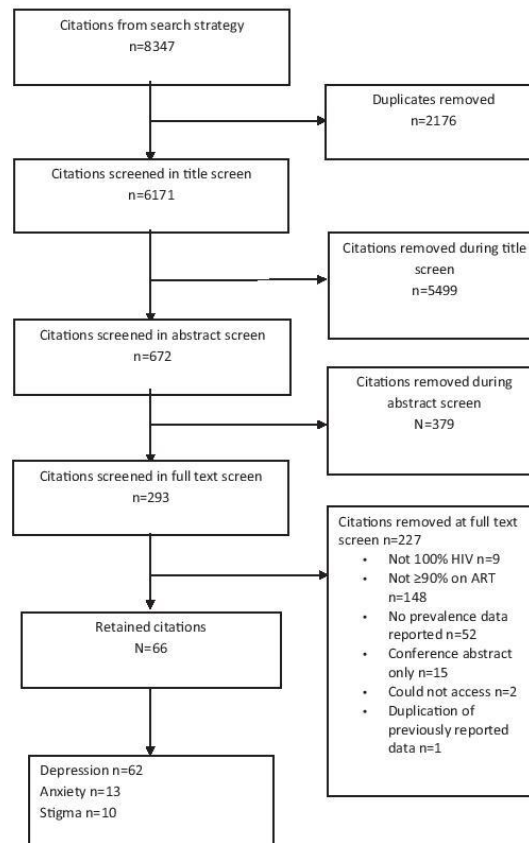


Fig. 1. PRISMA flow diagram.

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Table 2
Characteristics of retained citations.

Authors Reference list	Year of publication	High or low and middle income country	Country	Study objectives	Study design	Sample size	Depression anxiety or stigma	Prevalence	Loney data quality score
Adeyuya et al. (Adeyuya et al., 2009)	2009	Low or middle	Nigeria	To investigate correlates of post-traumatic stress disorder (PTSD) following intense stigmatising events in HIV infected individuals.	Cross-sectional	190	Stigma	61.6%	6
Adeyuya et al. (Adeyuya et al., 2008)	2008	Low or middle	Nigeria	To evaluate the association between clinical depression and quality of life in HIV positive subjects in Nigeria.	Cross-sectional	87	Depression	28.7%	6
Alciati et al. (Alciati et al., 2001)	2001	High	Italy	To assess the prevalence of current mood disorders in HIV positive patients treated with antiretroviral therapy.	Cross-sectional	90	Depression	6.30%	5
Ammassari et al. (Ammassari et al., 2004)	2004	High	Italy	To examine the association between antiretroviral therapy adherence and depressive symptoms.	Cross-sectional	135	Depression	24%	6
Bayon et al. (Bayon et al., 2012)	2012	High	Spain	To assess the prevalence of depressive symptoms, sleep disturbances, and subjective cognitive complaints in patients with HIV receiving antiretroviral therapy.	Cross-sectional	799	Depression	35.4%	7
Bhat et al. (Bhat et al., 2013)	2013	Low or middle	India	To assess the prevalence of depression in the patients with HIV infection	Cross-sectional	299	Depression	49.8%	4
Bhengu et al. (Bhengu et al., 2011)	2011	Low or middle	South Africa	To examine sociodemographic characteristics, symptoms, health, quality of life, and the impact reported by those taking antiretroviral therapy in South Africa.	Cross-sectional	149	Sadness	24%	4
Boarts et al. (Boarts et al., 2008)	2008	High	USA	To compare the distinct relationships of different types of discrimination to non-adherence among people living with HIV/AIDS.	Cohort study	57	Stigma	83%	3
Boarts et al. (Boarts et al., 2006)	2006	High	USA	To investigate the independent and co morbid influence of PTSD and depression symptoms on adherence.	Cohort study	57	Depression	49%	4
Bogart et al. (Bogart et al., 2010)	2010	High	USA	To investigate the simultaneous effects of discrimination from HIV-serostatus, race/ethnicity, and sexual orientation among HIV-positive black men who have sex with men.	Cohort study	181	Stigma	38%	3
Bongongo et al. (Bongongo et al., 2013)	2013	Low or middle	South Africa	To screen for depressive symptoms amongst HIV patients receiving antiretroviral therapy.	Cross-sectional	117	Depression	71.80%	6
Bouhnik et al. (Bouhnik et al., 2005)	2005	High	France	To examine the impact of adherence from that of injecting drug status and depressive syndrome on HIV clinical progression.	Cohort study	243	Depression	40.4%	7

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Table 2 (Continued)

Authors Reference list	Year of publication	High or low and middle income country	Country	Study objectives	Study design	Sample size	Depression anxiety or stigma	Prevalence	Loney data quality score
Braganca et al. (Braganca and Palha, 2011)	2011	High	Portugal	To test the hypotheses that depression and neurocognitive disorders are prevalent in this sample and that depression and its severity increases with cognitive deterioration.	Cross-sectional	130	Depression	34%	4
Buathong et al. (Buathong et al., 2009)	2009	Low or middle	Thailand	To estimate the prevalence of non-adherence to antiretroviral therapy and to determine the association of depression and related factors with adherence to antiretroviral therapy in Thai adult HIV-infected patients	Cross-sectional	379	Depression	32.3%	6
Campos et al. (Campos et al., 2009)	2009	Low or middle	Brazil	To identify factors associated with better levels of self reported quality of life after four months of antiretroviral therapy.	Cohort study	262	Anxiety, depression	51.5% anxiety, 40.6% depression	6
Cha et al. (Cha et al., 2008)	2008	High	USA	To examine the impact of perceived social support, depressive symptoms and medication-taking self-efficacy on self-reported medication adherence in persons with HIV	Cross-sectional	215	Depression	39%	5
Clarke et al. (Clarke et al., 2010)	2010	Low or middle	Jamaica	To test a hypothesis that there is a high prevalence of depression among persons living with HIV/AIDS and being treated in a specialist clinic in Kingston, Jamaica.	Cross-sectional	50	Depression	46%	4
Cohen et al. (Cohen et al., 2009)	2009	Low or middle	Rwanda	To measure trauma experiences of Rwandan women and identify predictors associated with PTSD and depressive symptoms	Cross-sectional	658	Depression	81.5%	6
Dasgupta et al. (Dasgupta et al., 2013)	2013	Low or middle	India	To describe stigma among women attending this clinic who are on antiretroviral therapy, and how this measure relates to access to HIV care.	Cross-sectional	198	Stigma	82%	5
de Souza et al. (de Souza et al., 2011)	2011	Low or middle	Brazil	To analyse self-rated health status and its association with sex, age, socioeconomic status and characteristics related to treatment among AIDS patients receiving antiretroviral therapy in Brazil.	Cross-sectional	1245	Anxiety and depression	54.1% depression, 39.6 anxiety	8
De et al. (De and Dalui, 2012)	2012	Low or middle	India	Assessment of factors influencing adherence to anti-retroviral therapy for human immunodeficiency virus positive mothers and their infected children.	Cross-sectional	94	Depression	100%	4

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Do et al. (Do et al., 2013)	2013	Low or middle	Vietnam	To assess the level of suboptimal adherence to antiretroviral therapy among PLHIV and examine the influence of a range of possible determinants of antiretroviral therapy adherence in Northern Vietnam.	Cross-sectional	615	Depression	78%	6
Do et al. (Do et al., 2010)	2010	Low or middle	Botswana	To determine which aspects of quality of life were negatively correlated with adherence.	Cross-sectional	300	Depression	28.3%	6
Farrant et al. (Farrant et al., 2012)	2012	Low or middle	South Africa	To measure the prevalence and burden of pain and other physical and psychological symptoms among South African HIV-positive patients attending highly active antiretroviral therapy clinics.	Cross-sectional	385	Sadness and worry	64.7% feeling sad, 61.0% worrying	6
Garvie et al. (Garvie et al., 2011)	2011	High	USA	To examine psychological factors and adherence to antiretroviral therapy of youth on directly observed therapy programme.	RCT (baseline data)	12	Depression	66%	3
Gaynes et al. (Gaynes et al., 2012)	2012	Low or middle	Cameroon	To determine the prevalence of clinically relevant depressive illness in HIV patients in a small urban setting in Cameroon.	Cross-sectional	400	Depression	Month 3% 6 months 5%, Year 7%, Lifetime 29%	6
Gibbie et al. (Gibbie et al., 2006)	2006	High	Australia	To assess changes in depression and neuropsychological performance over time, and to explore the relationship between depression, HIV infection and neuropsychological performance.	Cross-sectional	78	Depression	31%	7
Gonzalez et al. (Gonzalez et al., 2011a,b)	2011	High	USA	To examine measurement differences in the effect of depression on adherence.	Cross-sectional	91	Depression	92%	5
Gordillo et al. (Gordillo et al., 1999)	1999	High	Spain	To assess adherence and identify sociodemographic and psychological factors which may impact this.	Cross-sectional	366	Anxiety and depression	40.4% depression, 42.4% anxiety	7
Judd et al. (Judd et al., 2005)	2005	High	Australia	To assess whether distinct subtypes of depression can be related to the presence/absence of various psychological, social or cognitive factors.	Cross-sectional	129	Depression	34.8%	5
Keltner et al. (Keltner et al., 2012)	2012	High	USA	To assess the relative influence of depressed mood and pain on health related quality of life.	Cross-sectional	397	Depression	Lifetime 46%, Current 21%	6
Knowlton et al. (Knowlton et al., 2011)	2011	High	USA	To investigate gender difference in social support and its effect on antiretroviral therapy adherence.	Cross-sectional	154	Depression	33.12%	6
Kong et al. (Kong et al., 2012)	2012	High	USA	To examine the association between race and antiretroviral therapy adherence.	Cross-sectional	7034	Depression	46.7%	7
Lawler et al. (Lawler et al., 2011)	2011	Low or middle	Botswana	To determine the incidence of depression in an HIV-positive population in Botswana.	Cross-sectional	120	Depression	38%	5
Michel et al. (Michel et al., 2010)	2009	High	France	To assess to what extent depression and treating depressive can reduce the fatigue.	Cross-sectional	328	Depression	46.8%	7

Table 2 (Continued)

Authors Reference list	Year of publication	High or low and middle income country	Country	Study objectives	Study design	Sample size	Depression anxiety or stigma	Prevalence	Loney data quality score
Nakimuli-Mpungu et al. (Nakimuli-Mpungu et al., 2013)	2013	Low or middle	Uganda	To examine the association between lifetime depressive disorders and antiretroviral therapy adherence among a rural clinic-based HIV positive population.	Cross-sectional	400	Depression	Sub clinical 39.35%, Current 12.25%, Lifetime 23.75%	6
Nakimuli-Mpungu et al. (Nakimuli-Mpungu et al., 2011)	2011	Low or middle	Uganda	To explore prevalence of depression and covariates.	Cross-sectional	500	Depression	48% depression, Major 25%, Lifetime 15.2%	6
Nel et al. (Nel and Kagee, 2013)	2013	Low or middle	South Africa	To determine the severity of symptoms of depression and anxiety among a South African sample of patients receiving antiretroviral therapy in a public HIV clinic.	Cross-sectional	96	Anxiety and depression	40.4% depression, 28.7% anxiety	4
Nozaki et al. (Nozaki et al., 2011)	2011	Low or middle	Zambia	To examine the correlates of non adherence to antiretroviral therapy	Cross-sectional	518	Stigma	16% related to ART	5
Nurutdinova et al. (Nurutdinova et al., 2012)	2012	High	USA	To assess the impact of mental health diagnosis on progression to AIDS defining illness or death.	Cohort study	9003	Anxiety and depression	Depression 41, Anxiety 18%	6
Nyamathi et al. (Nyamathi et al., 2013)	2013	Low or middle	India	To examine whether an intervention will decrease internalised stigma and avoidant coping at 6-month follow-up.	Randomised controlled trial (baseline data)	68	Depression	54.4%	5
Olagunju et al. (Olagunju et al., 2012)	2012	Low or middle	Nigeria	To determine the prevalence as well as types of anxiety disorders among PLWHA, and describe the correlates of anxiety disorders in them.	Cross-sectional	300	Anxiety	21.70%	7
Olisah et al. (Olisah et al., 2011)	2011	Low or middle	Nigeria	To determine the frequency of depressive disorder in a sample of patients with HIV and its level of under-diagnosis by attending physicians.	Cross-sectional	310	Depression	21.3% (CES-D), 14.2% met criteria for SCAN	6
Owolabi et al. (Owolabi et al., 2012)	2012	Low or middle	Nigeria	To assess stigma and discrimination experienced by people living with HIV/ AIDS.	Cross-sectional	300	Stigma	25.3%	4
Palmer et al. (Palmer et al., 2011)	2011	High	Canada	To explore the factors related to positive body image among a cohort of antiretroviral therapy recipients in British Columbia.	Cross-sectional	451	Depression and stigma	46% stigma, 57% depression	7
Pappin et al. (Pappin et al., 2012)	2012	Low or middle	South Africa	To assess the impact of social, demographic and health variables on anxiety and depression antiretroviral therapy patients in the Free State Province of South Africa.	Cross-sectional	499	Anxiety and depression	Anxiety 30.6%, depression 25.4%	7
Peretti-Watel et al. (Peretti-Watel et al., 2006)	2006	High	France	To investigate patterns of HIV disclosure to different kinds of significant others.	Cross-sectional	2932	Stigma	Relatives 12.9%, friends 12.2%, sexual partners 16.3%	7
Peterson et al. (Peterson et al., 2012)	2012	Low or middle	Gambia	To establish the prevalence of positive screening tests for depression and PTSD among patients on antiretroviral therapy.	Cross-sectional	252	Depression	6%	6

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Poupard et al. (Poupard et al., 2007)	2007	Low or middle	Senegal	To evaluate the quality of life and prevalence of depression among patients treated for $\geq 6/12$ antiretroviral therapy.	Cross-sectional	200	Depression	18%	5
Pumpradit et al. (Pumpradit et al., 2010)	2010	Low or middle	Thailand	To determine the frequency of neuro cognitive impairment and psychiatric co morbidity among Thais with undetectable viral load.	Cross-sectional	64	Anxiety and depression	4.7% depression, 0% anxiety	4
Rabkin et al. (Rabkin et al., 2000)	2000	High	USA	To determine whether apathy is associated with neurocognitive symptoms and/or depressive symptoms in HIV/AIDS and also adherence.	Cross-sectional	58	Depression	Current 7%, lifetime 55%	3
Roux et al. (Roux et al., 2009)	2009	High	France	To assess whether psychiatric illness affects adherence to antiretroviral therapy differently in men or women.	Cross-sectional	1809	Anxiety and depression	Anxiety 63% women, 49% men Depression 24% women, 22% men 48%	7
Sarna et al. (Sarna et al., 2008)	2008	Low or middle	India	To investigate levels of adherence to treatment among PLHA receiving antiretroviral therapy in India.	Cross-sectional	310	Depression		6
Schoesson et al. (Schoesson et al., 2007)	2007		Sweden	To assess the degree of suboptimal adherence to dose the effects of personal factors.	Cross-sectional	193	Anxiety	48%	5
Silveira et al. (Silveira et al., 2012)	2012	Low or middle	Brazil	To report the prevalence of depressive symptoms and to identify associated risk factors in patients on antiretroviral therapy.	Cross-sectional	246	Depression	32% (95% CI 26–40)	7
Simoni et al. (Simoni et al., 2007)	2007	High	USA	To evaluate a peer support intervention on depressive symptoms in non-adherence.	Randomised controlled trial (baseline data)	136	Depression	52%	5
Starace et al. (Starace et al., 2002)	2002	High	Italy	To examine the association between taking antiretroviral therapy and neuropsychiatric disorders.	Cohort study (cross-sectional data)	268	Depression	14.1%	6
Sumari-de Boer et al. (Sumari-de Boer et al., 2012)	2012	High	Netherlands	To compare adherence to antiretroviral therapy and treatment response risk factors for non-adherence.	Cross-sectional	201	Depression	27%	5
Tucker et al. (Tucker et al., 2003)	2003	High	USA	To examine the associations of mental health and substance use problems with adherence	Cohort	1910	Anxiety and depression	20% depression 3% anxiety	6
Wagner et al. (Wagner et al., 2011)	2011	High	USA	To examine the relationship between depression and adherence.	Cohort	1374	Depression	43%	7
Wolfe et al. (Wolfe et al., 2006)	2006	Low or middle	Botswana	To investigate the role of stigma as a potential barrier to the diagnosis and treatment of HIV.	Cross-sectional	112	Stigma	12% non disclosure, 30% personal relationships, 27% fear unemployment, 47% difficulty with work	3
Wolitski et al. (Wolitski et al., 2009)	2009	High	USA	To test the hypothesis that higher levels of internal, perceived external, and total HIV-related stigma would be associated with poorer physical and mental health and associated health behaviours.	Randomised controlled trial (baseline data)	637	Stigma	Complex-summarised in results	7
Wouters et al. (Wouters et al., 2012)	2012	Low or middle	South Africa	To determine the preferred factor structure of the HADS in particularly vulnerable patient groups.	Cross-sectional	716	Anxiety and depression	31.3% anxiety, 25.4% depression	6

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Table 2 (Continued)

Authors Reference list	Year of publication	High or low and middle income country	Country	Study objectives	Study design	Sample size	Depression anxiety or stigma	Prevalence	Loney data quality score
Yen et al. (Yen et al., 2004)	2004	Low or middle	China	To identify the quality of life in Taiwanese HIV/AIDS male outpatients receiving antiretroviral therapy.	Cross-sectional	41	Depression	41.5%	5
Zhang et al. (Zhang et al., 2012)	2012	High	Canada	To validate a shortened version of the Centre for Epidemiological Survey's depression scale (CES-D).	Cross-sectional	563	Depression	51%	6

conducted extremely conservatively. Many citations were updates on new formulations or reports of toxicities of antiretroviral therapy, opinion pieces, or editorials, or it was made apparent in the title that the citation was a systematic review or would otherwise not contain any new original research data.

3.1. Characteristics of eligible papers

66 citations were retained after application of the inclusion and exclusion criteria. 48% ($n = 32$) of papers reported data from high income countries (USA ($n = 16$), France ($n = 4$), Italy ($n = 3$), Australia ($n = 2$), Canada ($n = 2$), Spain ($n = 2$), Netherlands, Portugal and Sweden (all $n = 1$)) and 34 papers reported data from low and middle income countries (South Africa ($n = 6$), India ($n = 5$), Nigeria ($n = 5$), Botswana ($n = 3$), Brazil ($n = 3$), Thailand ($n = 2$), Uganda ($n = 2$), Cameroon, China, Gambia, Jamaica, Rwanda, Senegal, Vietnam and Zambia (all $n = 1$)).

3.2. Data quality

The quality of the included papers is summarised in Table 3 according to Loney et al. (1998). Over a half (57.5%) of papers scored 6 or more out of a possible score of 8, indicating a generally high level of data quality.

3.3. Study design, tools and measures

Among the retained citations, four reported baseline data from randomised controlled trials, nine were data from cohort studies and 53 (80%) were cross-sectional studies.

The most commonly used tools to assess depression were the Beck Depression Index (BDI) ($n = 16$), the Centre for Epidemiological Studies depression tool (CES-D) ($n = 15$) and the Hospital Anxiety and Depression Scale (HADS) ($n = 5$). Twenty-six other measurement tools were used to assess depression. The most common tool used to measure anxiety was the HADS ($n = 5$). Eight other tools were used to measure anxiety.

The measurement of stigma is complex, as stigma is a socially constructed phenomenon and therefore expressed differently in different cultural and social contexts. Of the ten citations relating to levels of stigma retained after exclusion criteria were applied, three studies used a modified version of the Berger stigma scale, four used a locally designed questionnaire, two used discrimination scales not specific to HIV and one used a modified version of the Mini International Neuropsychiatric Interview (MINI).

3.4. Prevalence ranges

3.4.1. Depression

A total of 62 retained citations reported mean sample prevalence for depression (summarised in Table 4). The range of reported depression prevalence is illustrated by Fig. 2 for all retained citations and by country income status.

The weighted mean of point prevalence of depression in people with HIV on antiretroviral therapy across the

Table 3
Data quality summary (using Loney et al., 1998).

Loney critical appraisal score	n (%)	High income countries (n = 32), n (%)	Low and middle income countries (n = 34), n (%)	References
1	0	0	0	–
2	0	0	0	–
3	5 (7.6)	4 (12.5)	1 (2.9)	Boarts et al. (2008), Bogart et al. (2010), Garvie et al. (2011), Rabkin et al. (2000) and Wolfe et al. (2006)
4	9 (13.6)	2 (6)	7 (20.6)	Bhat et al. (2013), Bhengu et al. (2011), Boarts et al. (2006), Braganca and Palha (2011), Clarke et al. (2010), De and Dalui (2012), Neland Kagee (2013), Owolabi et al. (2012), and Pumpradit et al. (2010)
5	14 (21.2)	8 (25)	6 (17.6)	Alciati et al. (2001), Cha et al. (2008), Dasgupta et al. (2013), Edelman et al. (2012), Gonzalez et al. (2011a,b), Judd et al. (2005), Lawler et al. (2011), Nozaki et al. (2011), Nyamathi et al. (2013), Poupard et al. (2007), Schoesson et al. (2007), Simoni et al. (2007), Sumari-de Boer et al. (2012) and Yen et al. (2004)
6	23 (34.8)	7 (21.9)	16 (47.1)	Adewuya et al. (2009), Adewuya et al. (2008), Ammassari et al. (2004), Bongongo et al. (2013), Buathong et al. (2009), Campos et al. (2009), Cohen et al. (2009), Do et al. (2013), Do et al. (2010), Farrant et al. (2012), Gaynes et al. (2012), Keltner et al. (2012), Knowlton et al. (2011), Nakimuli-Mpungu et al. (2013), Nakimuli-Mpungu et al. (2011), Nurutdinova et al. (2012), Olisah et al. (2011), Peterson et al. (2012), Sama et al. (2008), Starace et al. (2002), Tucker et al. (2003), Wouters et al. (2012) and Zhang et al. (2012)
7	14 (21.2)	11 (34.4)	3 (8.8)	Bayon et al. (2012), Bouhnik et al. (2005), Gibbie et al. (2006), Gordillo et al. (1999), Kong et al. (2012), Michel et al. (2010), Olagunju et al. (2012), Palmer et al. (2011), Pappin et al. (2012), Peretti-Watel et al. (2006), Roux et al. (2009), Silveira et al. (2012), Wagner et al. (2011) and Wolitski et al. (2009)
8	1 (1.5)	0	1 (2.9)	de Souza et al. (2011)

citations retained was 33.6%, with a higher point prevalence of depression reported in low and middle income countries (41.36%) compared with high income countries (25.81%). Period prevalence, combining data over the past week to month was, as expected, higher. The period prevalence weighted mean was 39.8% in all retained citations, 41.0% in high income countries, and 38.7% in low and middle income countries. Fewer studies reported rates for depression over the lifetime, or in the past 6 months, and so the data were merged to reports of depression in the longer term (6 months to lifetime). The difference in reported 6 months to lifetime depression comparing high income countries and low and middle income countries is noteworthy, although there was strong potential for bias due to the small numbers of papers reporting this data.

From the scatter plots several outliers are evident. These outliers appear to originate in more homogenous and possibly more unusual samples than the general HIV population. The data reporting 100% one-week period prevalence of depression was among mothers who were attending an outpatient clinic with their HIV positive children (De and Dalui, 2012). The sample reporting 92% one-week period prevalence of depression was composed of people who used to inject drugs (Gonzalez et al., 2011a,b). The sample which reported 81.5% one-week prevalence of depression was composed of Rwandan women experiencing post genocidal trauma (Cohen et al., 2009). All of these samples would be expected to experience more psychological distress. Most other samples were more heterogeneous and contained a mix

of people who inject drugs, men who have sex with men, and other groups at risk of infection.

Prevalence for each risk behaviour group (people who inject drugs, heterosexual women, men who have sex with men, former plasma or blood donors) was not disaggregated within the data reported; therefore a comparison of these sub-groups was not possible. As described, the data were presented by country income status as a proxy indicator of generalised or focused epidemics.

Analysis by measurement tool was possible only for point prevalence as period prevalence was usually not measured using standardised tools. The most commonly used measures were the Beck Depression Inventory (BDI), the CES-D (Centre for Epidemiological Studies depression tool) and the Hospital Anxiety and Depression scale (HADS). The range of prevalence and mean (again, weighted by data quality score) from the BDI, CES-D and the HADS data are presented in Fig. 3. Data from the HADS appears to report lower prevalence of depression.

3.4.2. Anxiety

In total 14 papers reported the prevalence of anxiety in a study sample. Data are summarised in Table 5 and the range of reported prevalence illustrated in Fig. 4.

The mean point prevalence of anxiety was 28.38%; this was lower in high income countries (21.53%) compared with low and middle income countries (33.92%). One to four weeks period prevalence was higher at 33.59%; this was higher in high income countries (39.55%) compared with low and middle income countries (21.18%).

Table 4
Summary of depression prevalence for all citations and by country income status.

Depression (all means weighted by data quality score)			
	Mean (SD)	High income countries (SD)	Low and middle income countries (SD)
Point prevalence (n = 14) Included studies	33.60 (19.47) Alciati et al. (2001), Ammassari et al. (2004), Bhengu et al. (2011), Bongongo et al. (2013), Braganca and Palha (2011), de Souza et al. (2011), Kong et al. (2012), Lawler et al. (2011), Nakimuli-Mpungu et al. (2013), Nakimuli-Mpungu et al. (2011), Nurutdinova et al. (2012), Rabkin et al. (2000), Starace et al. (2002) and Tucker et al. (2003)	25.81 (15.21) Alciati et al. (2001), Ammassari et al. (2004), Braganca and Palha (2011), Kong et al. (2012), Nurutdinova et al. (2012), Rabkin et al. (2000), Starace et al. (2002) and Tucker et al. (2003)	41.36 (21.42) Bhengu et al. (2011), Bongongo et al. (2013), de Souza et al. (2011), Lawler et al. (2011), Nakimuli-Mpungu et al. (2013) and Nakimuli-Mpungu et al. (2011)
Period prevalence of 1 week to 1 month (n = 41) Included studies	39.79 (21.52) Adewuya et al. (2008), Bayon et al. (2012), Bhat et al. (2013), Boarts et al. (2006), Bouhnik et al. (2005), Buathong et al. (2009), Campos et al. (2009), Cha et al. (2008), Clarke et al. (2010), Cohen et al. (2009), De and Dalui (2012), Do et al. (2013), Do et al. (2010), Farrant et al. (2012), Garvie et al. (2011), Gaynes et al. (2012), Gibbie et al. (2006), Gonzalez et al. (2011a,b), Gordillo et al. (1999), Judd et al. (2005), Keltner et al. (2012), Knowlton et al. (2011), Michel et al. (2010), Nel and Kagee (2013), Nyamathi et al. (2013), Olisah et al. (2011), Palmer et al. (2011), Pappin et al. (2012), Peterson et al. (2012), Poupard et al. (2007), Pumpradit et al. (2010), Roux et al. (2009), Sarna et al. (2008), Silveira et al. (2012), Simoni et al. (2007), Sumari-de Boer et al. (2012), Wagner et al. (2011), Wouters et al. (2012), Yen et al. (2004) and Zhang et al. (2012)	40.96 (17.08) Bayon et al. (2012), Boarts et al. (2006), Bouhnik et al. (2005), Cha et al. (2008), Garvie et al. (2011), Gibbie et al. (2006), Gonzalez et al. (2011a,b), Gordillo et al. (1999), Judd et al. (2005), Keltner et al. (2012), Knowlton et al. (2011), Michel et al. (2010), Palmer et al. (2011), Roux et al. (2009), Simoni et al. (2007), Sumari-de Boer et al. (2012), Wagner et al. (2011) and Zhang et al. (2012)	38.69 (25.07) Adewuya et al. (2008), Bhat et al. (2013), Buathong et al. (2009), Campos et al. (2009), Clarke et al. (2010), Cohen et al. (2009), De and Dalui (2012), Do et al. (2013), Do et al. (2010), Farrant et al. (2012), Gaynes et al. (2012), Nel and Kagee (2013), Nyamathi et al. (2013), Olisah et al. (2011), Pappin et al. (2012), Peterson et al. (2012), Poupard et al. (2007), Pumpradit et al. (2010), Sarna et al. (2008), Silveira et al. (2012), Wouters et al. (2012) and Yen et al. (2004)
Period prevalence of 6 weeks to lifetime (n = 7) Included studies ^a	23.61 (19.03) Gaynes et al. (2012), Keltner et al. (2012), Nakimuli-Mpungu et al. (2013), Nakimuli-Mpungu et al. (2011) and Rabkin et al. (2000)	49.0 (6.36) Keltner et al. (2012) and Rabkin et al. (2000)	15.99 (10.39) Gaynes et al. (2012), Nakimuli-Mpungu et al. (2013) and Nakimuli-Mpungu et al. (2011)

^a Several studies contributed more than one prevalence period, e.g. lifetime, one year and 6 months, so numbers may not add up to total number of studies.

Women in a French cross-sectional study reported the highest prevalence of anxiety (63% anxiety) (Roux et al., 2009). Men in the same study reported a prevalence of 48% anxiety (Roux et al., 2009). The lowest prevalence of anxiety (0%) was in a Thai sample (Pumpradit et al., 2010). The authors suggest that this low prevalence of anxiety could have been the result of strong social support among people with HIV/AIDS attending the clinic where recruitment occurred, which may serve to reduce anxiety.

3.4.3. Stigma

Prevalence of stigma was reported in ten papers. Of these, seven reported an overall summarising prevalence

figure for the presence or absence of the experience of stigma in the study sample (see Table 6).

The remaining three studies all used locally designed questionnaires, measuring different aspects of the experience of stigma. A study in Zambia focused on the experience of stigma specifically related to antiretroviral therapy, reporting a prevalence of 16% (Nozaki et al., 2011). A national cross-sectional survey including HIV positive patients in France reported percentage experiencing discrimination; 12.9% from relatives, 12.2% from friends and 16.3% from sexual partners (Peretti-Watel et al., 2006). A study conducted in Botswana in 2006, before widespread access to antiretroviral therapy, found that 12% of HIV

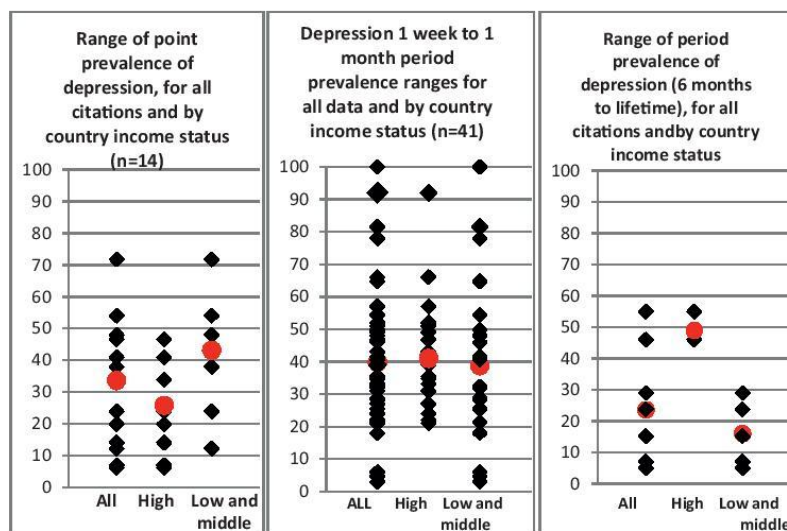


Fig. 2. Scatter plots to illustrate the range and distribution of reported prevalence of depression. All means weighted by data quality score. ● = weighted mean.

patients had not disclosed their infection status to anyone. In the same study 27% of patients feared they would lose their job due to HIV, and 47% reported work-related difficulties due to HIV, mostly concerned with taking sick leave (Wolfe et al., 2006).

4. Discussion

This review has synthesised the data for depression, anxiety and stigma among HIV positive patients on antiretroviral therapy. The literature available was of high quality, although heterogeneous with respect to methodologies, sample characteristics and assessment tools.

Despite these limitations, the data presented provides a broader understanding of depression, anxiety and stigma in HIV positive people on antiretroviral therapy.

4.1. Depression

A mean point prevalence of 33.60% (SD 19.47) depression was identified in this review, and a 1–4 weeks period prevalence of 39.79% (SD 21.52). The data for longer period prevalence was sparse and therefore the mean of this data is less likely to be representative of the population. The UK general adult population data for prevalence of depression ranges from 2.3% (HSCIC, 2009) to 8.1% (ONS, 2010). General population data from Nigeria reports a 5.2% point prevalence (Amaran et al., 2007), the USA 9.5% 12-month prevalence (Kessler et al., 2005), South Africa a 9.7% period prevalence for lifetime depression and 4.9% for the past 12 months (Tomlinson et al., 2009), and in the Asia Pacific region figures stand at 1.3% to 5.5% current to 1 month prevalence of depression (Chiu, 2004). This suggests that depression is elevated in HIV positive people in comparison with international general population data.

In Table 7, other chronic conditions are compared with HIV for prevalence of depression. Conditions were chosen as suitable comparators as they are associated with incurability, physical symptoms and long-term management using medication. The prevalence of depression is highest in people living with HIV compared with these other conditions.

Recent international comparisons of the impact of depression on disability adjusted life years and years lived with disability indicate that the global burden of depression is higher in low and middle income countries

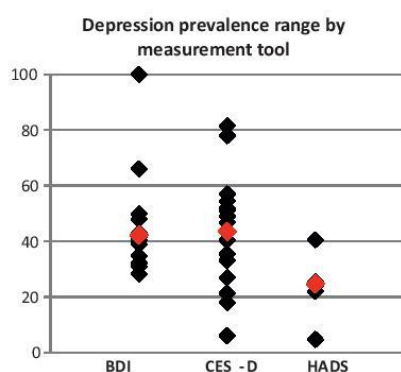


Fig. 3. One-four week period prevalence of depression by outcome measure. All means weighted by data quality score. ● = weighted mean.

Table 5

Summary of prevalence of anxiety for all retained citations and by country income status.

Anxiety (all means weighted by data quality score)			
	Mean (SD)	High income countries mean (SD)	Low and middle income countries mean (SD)
Point prevalence (n = 6) Included studies	28.38 (17.07) Campos et al. (2009), de Souza et al. (2011), Nurutdinova et al. (2012), Olagunju et al. (2012), Schoesson et al. (2007) and Tucker et al. (2003)	21.53 (22.91) Nurutdinova et al. (2012), Schoesson et al. (2007) and Tucker et al. (2003)	33.92 (10.64) Campos et al. (2009), de Souza et al. (2011) and Olagunju et al. (2012)
1–4 weeks period prevalence (n = 8) Included studies	33.59 (21.07) Edelman et al. (2011), Gordillo et al. (1999), Nel and Kagee (2013), Pappin et al. (2012), Pumpradit et al. (2010), Roux et al. (2009) and Wouters et al. (2012)	39.55 (24.640) Edelman et al. (2011), Gordillo et al. (1999) and Roux et al. (2009)	21.18 (14.28) Nel and Kagee (2013), Pappin et al. (2012), Pumpradit et al. (2010) and Wouters et al. (2012)

compared with high income countries (Ferrari et al., 2013). A similar difference was identified in this review (point prevalence in high income countries 25.81% (SD 15.21) vs. low and middle income countries 41.36% (SD 21.42)). These data suggest that depression is higher in HIV positive people than in the general population, and that depression is more burdensome in low and middle income countries than in high income countries.

4.2. Anxiety

A recent systematic review identified a global prevalence of anxiety of 7.3% in the general population, with a lower prevalence in African countries (5.3%) compared to Euro/Anglo cultures (10.4%) (Baxter et al., 2012). The prevalence of anxiety disorders in the general population is 4.4% in the UK (HSCIC, 2009) and 18.1% in the US (Kessler et al., 2005). Whilst there is variation in these figures, they are all much lower than the prevalence identified in this review amongst people with HIV on antiretroviral therapy: 28.38% (SD 17.07) mean point prevalence and 33.59% (SD 21.07) 1–4 week period prevalence.

The prevalence of anxiety among patient with HIV receiving antiretroviral therapy identified in this review is

also high in comparison with rates of anxiety among patients with other chronic conditions (Clarke and Currie, 2009), suggesting that people with HIV/AIDS are at a higher risk of developing anxiety than other patients with chronic conditions (Table 8).

4.3. Stigma

We found that the prevalence of depression and anxiety are higher in HIV positive populations compared with the general population and patients with other chronic conditions. This could be due to the stigmatising beliefs associated with HIV infection, such as that people living with HIV are immoral or unsafe to be associated with (Deacon, 2006; Parker and Aggleton, 2003). Experiences of stigma are strongly associated with psychosocial distress in the literature (Simbayi et al., 2007; Stutterheim et al., 2009).

The data extracted from the retained citations on stigma suggests that from 42% to 83% of people with HIV on antiretroviral therapy experience some type of stigma. This includes discrimination from friends, family or community and also internalised feelings of stigma associated with poor self worth related to an HIV diagnosis.

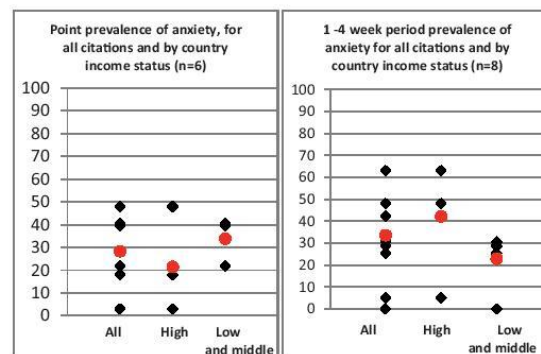


Fig. 4. Scatter plots to illustrate the range and distribution of reported prevalence of anxiety. All means weighted by data quality score. ● = weighted mean.

Table 6
Summary of prevalence of experience of stigma for all citations and by country income status.

	All data	High income countries	Low and middle income countries
Point prevalence	41.92%, 46%, 82%	41.92%, 46%	82%
Included studies	Dasgupta et al. (2013), Palmer et al. (2011) and Wolitski et al. (2009)	Palmer et al. (2011) and Wolitski et al. (2009)	Dasgupta et al. (2013)
In the last 2 weeks	61.6%	–	61.6%
Included studies	Adewuya et al. (2009)		Adewuya et al. (2009)
From 'during the past year' to 'ever'	38%, 25.3%, 83%	83%, 38%	25.3%
Included studies	Boarts et al. (2008), Bogart et al. (2010) and Owolabi et al. (2012)	Boarts et al. (2008) and Bogart et al. (2010)	Owolabi et al. (2012)

Table 7
Comparison of prevalence of depression with HIV positive people on ART and other chronic conditions.

Population (prevalence period)	Depression prevalence
HIV positive people on antiretroviral therapy (current or 1–4 weeks)	33.6–39.8% (this review)
Epilepsy patients (current or past year)	23.1% (Fiest et al., 2012)
Multiple sclerosis patients (1 year period)	25.7% (Patten et al., 2003)
Patients with diabetes (not stated)	28% women 18% men (Anderson et al., 2001)

Table 8
Comparison of prevalence of anxiety with HIV positive people on ART and other chronic conditions.

Population	Anxiety prevalence
HIV positive people on antiretroviral therapy (current or 1–4 weeks)	28.3–33.6% (this review)
Patients with diabetes (current)	14% (Clarke and Currie, 2009)
Patients with cancer (current)	15–23% (Clarke and Currie, 2009)
Patients with heart disease (current panic disorder)	10–50% (Clarke and Currie, 2009)

However, stigma is a complex and multifaceted concept, expressed and experienced differently in different cultural contexts, therefore it cannot be assumed that the same understanding or construct of stigma is being reported across studies. In addition, stigma can be described as enacted in the form of discrimination normative (a set of accepted values embedded in cultural norms), or internalised, meaning that the stigmatising messages are accepted by patients (Steward et al., 2008). This difference is not clearly defined in the retained citations. Although elements of these constructs are described by the stigma scales used in the identified studies, the interactions between stigma and the experience of discrimination are not explicit. For example, the literature states that the experience of stigma is often worse when patients have disclosed their serostatus, but does not specify levels of felt stigma in the society, which may dissuade people from disclosing and thus protect them from enacted stigma (Wolitski et al., 2009).

To add to the complexity, people living with HIV in high income countries may experience 'compound' or 'layered' stigma, where stigma exists along pre-existing social fault lines, on top of stigma related to sexual orientation, intravenous drug use, or commercial sex work (Campbell and Deacon, 2006; Nyblade, 2006). This creates difficulty when comparing experiences of stigma between high income countries and low and middle income countries, where stigma is mostly associated with women and sexual

morality, and begs the question of whether this kind of comparison is justified (Campbell et al., 2007).

There is a lack of accurate measures of stigma able to identify and measure felt, enacted, internalised stigma and compound or layered stigma (Nyblade, 2006). The People Living with HIV Stigma Index is an initiative by and for people living with HIV to collect information about stigma discrimination and human rights (International Planned Parenthood Federation, 2008). It was developed by a multi-agency group to be used to monitor trends over time, enable cross country comparison, and to provide an evidence base for programme and policy development. It thus represents a significant development for the future harmonisation of this literature, and the quality and reliability of future data.

4.4. Limitations

There were several methodological limitations encountered in this review. As described previously, sample characteristics such as gender, age, education level, socioeconomic status and virus transmission route all affect life experience, and therefore the prevalence of depression, anxiety and the experience of stigma. The reported data do not differentiate between these characteristics, and therefore the prevalence values reported encompass many different sub-populations within the HIV population. An attempt to differentiate between generalised and concentrated epidemics was made by

comparing the countries by income status, but this is a proxy indicator risk group, and cannot accurately reflect the complexities of cultural, social and economic contexts.

There are further limitations to the data reported on the prevalence of the experience of stigma. Exclusion criteria for this review indicated that papers with less than 90% of respondents on antiretroviral therapy should be excluded. There is limited evidence that the availability of antiretrovirals actually affects the levels of stigma in a community, therefore, this review might have been more comprehensive if all patients, regardless of treatment status, were included (Campbell et al., 2011).

A future review might stratify reported prevalence by year of access to antiretroviral therapy (i.e. Botswana 2004, Brazil 1996 and China 2002) to examine for effect of availability of antiretrovirals on depression, anxiety and experience of stigma or discrimination.

Data quality assessment was performed using a tool to evaluate the quality of health literature reporting prevalence or incidence and therefore was designed to suit the purpose of this review. However, whilst an item about standard measures was included, this review compares data from diverse cultural contexts and therefore it is essential that the measure is not only standardised, but also validated in this population. Assessment of the validity of the measures used in the identified studies was not included in the data quality assessment and this is a limitation to the findings of the review.

4.5. Clinical implications

Leaving psychosocial problems unaddressed may have major clinical and public health consequences. Recent review data suggests that depression (Gonzalez et al., 2011a,b) is strongly associated with decreased adherence, which is recognised to increase infectiousness, viral resistance and potential treatment failure (Bangsberg et al., 2000). This is especially hazardous in low or middle income countries, as fewer options are available as second or third line treatment, due to financial and logistical constraints. In order maintain first line treatment options, and as a therapeutic goal in itself, it is essential to address these psychological and social problems with holistic multidimensional support.

4.6. Future research

The lack of data in the literature on children and adolescents highlights a serious gap in the evidence regarding the psychosocial symptom burden experienced by this group of HIV patients on antiretroviral therapy and an area where further research is needed. Reporting by transmission route or by risk group behaviour would enable comparison between risk groups which would further inform screening policy in clinical practice. In addition, the development, validation and consistent use of a multidimensional assessment tool to assess symptom prevalence would reduce methodological challenges related to the assessment and classification of conditions, as well as reflecting a more holistic conception of health endorsed by the WHO (1948). Future research should also

concentrate on the effectiveness of interventions to address depression, anxiety and stigma, now that the extent of problems is more fully understood. Recent systematic reviews have reviewed the evidence for potential treatment options for depression and anxiety in HIV infected people (Clucas et al., 2011; Sherr et al., 2011).

The holistic philosophy of palliative care is one possible response which could address these needs. Evidence from the pre-antiretroviral therapy era suggests that this person-centred approach, with multidisciplinary input, is effective in reducing pain, other symptoms and anxiety and improving spiritual wellbeing and HIV insight (Harding et al., 2005). It is also in line with WHO and UNAIDS policy and major international donors' recommendations, which state that palliative care should be made a priority in the care of HIV positive patients, delivered alongside other management options (PEPFAR, 2006; UCAID, 2011; UNAIDS, 2010a,b; WHO, 2004, 2012a,b). The effectiveness of palliative care should be assessed in the post-antiretroviral therapy era, bearing in mind that none of the papers in this review reported that patients were receiving care modelled on a holistic approach. This need for palliative care is not only recognised by funders and policy makers, but also increasing in clinical practice, where an integrated approach to care to avoid unnecessary suffering is mandated as an ethical imperative (Simms et al., 2012).

5. Conclusions

The prevalence of depression and anxiety in HIV positive people on antiretroviral therapy is higher than that of the general population and also in other chronic incurable conditions. Point prevalence of depression and anxiety in HIV populations on antiretroviral therapy are higher in low and middle income countries compared with high income countries. The one to four week period prevalence of anxiety is higher in high income countries but period prevalence of depression is comparable between high income countries and low and middle income countries. Over half of HIV positive people on antiretroviral therapy experience stigma.

Findings from this review suggest that in clinical practice, screening and assessment is needed to identify unmet multidimensional needs of HIV positive patients on antiretroviral therapy. It is feasible and reasonable that health care providers allocate resources to integrate holistic assessment into care packages in HIV clinics, in line with international policy and recommendations.

Authors contribution

KL conceived and designed the study and wrote the article with support from RH and LS, who with IJH also revised previous drafts for important intellectual content. IJH, RH, and LS all gave final approval for the version submitted.

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Conflicts of interest
None.

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Ethical approval

Not required.

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Appendix 4 – Ethical approvals

Ethical approval form from KEMRI



KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840 - 00200 NAIROBI, Kenya
Tel: (254) (020) 2722541, 2713349, 0722-205901, 0733-400003; Fax: (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website:www.kemri.org

KEMRI/RES/7/3/1

March 15, 2011

TO: DR. RICHARD HARDING (PRINCIPAL INVESTIGATOR)
DEPARTMENT OF PALLIATIVE CARE, POLICY & REHABILITATION

ATTN: DR. ZIPPORAH ALI,
NATIONAL CO-ORDINATOR,
KEHPCA

RE: NON-SSC PROTOCOL NO. 274 (RE-SUBMISSION): TOPCare
TREATMENT AND OUTCOMES IN PALLIATIVE CARE: RANDOMIZED
CONTROL TRIAL

Make reference to your letter dated 15th March, 2011 received on 16th March, 2011. Thank you for your response to the issues raised by the Committee. This is to inform you that the issues raised during the 186th meeting of the KEMRI/ERC meeting held on 15th February 2011, have been adequately addressed.

Due consideration has been given to ethical issues and the study is hereby granted approval for implementation effective this **15th day of March 2011**, for a period of twelve (12) months.

Please note that authorization to conduct this study will automatically expire on **14th March 2012**. If you plan to continue with data collection or analysis beyond this date, please submit an application for continuing approval to the ERC Secretariat by **14th December 2011**.

You are required to submit any amendments to this protocol and other information pertinent to human participation in this study to the ERC prior to initiation. You may embark on the study.

Yours sincerely,

ROKithinji
Caroline Kithinji,
FOR: SECRETARY,
KEMRI/NATIONAL ETHICS REVIEW COMMITTEE

Ethical approval form from Kings College London

Research Ethics Office

5.11 Franklin-Wilkins Building
(Waterloo Bridge Wing)
Stamford Street
London SE1 9NH
Tel 020 7846 4077/4070/4020
Email rec@kcl.ac.uk
www.kcl.ac.uk/research/ethics



Dr Richard Harding
Department of Palliative Care, Policy & Rehabilitation
School of Medicine
Cicely Saunders Institute
King's College London
Cutcombe Road
Denmark Hill
London SE5 9PJ

01 March 2011

Dear Dr Harding

BDM/10/11-31 TOPCare: Treatment and Outcomes in Palliative Care: A randomised controlled trial.

Thank you for sending in the amendments requested to the above project. I am pleased to inform you that these meet the requirements of the BDM RESC and therefore that full approval is now granted with the following provisos:

1. King's College London's research ethics approval is conditional on the study also being granted full ethical approval from the University of Nairobi, University of Cape Town and Ministry of Western Cape. Please ensure that you submit written evidence of full ethical approval from the University of Nairobi, University of Cape Town and Ministry of Western Cape to the Research Ethics Office once these have been received. The study must not commence until ethical approval from all of the above has been granted.
2. On the Information Sheet, please ensure you spell out what the abbreviation 'TOPCare' stands for the first time it is mentioned.
3. We note that you have responded 'yes' to Section D of the Risk Checklist, but have not addressed the related issues in Section 6.3. However, we note that you have addressed these issues sufficiently in Sections 6.4 and 6.5. For any future applications, please ensure you include your responses in the relevant sections of the application form.

Please ensure that you follow all relevant guidance as laid out in the King's College London Guidelines on Good Practice in Academic Research (<http://www.kcl.ac.uk/college/policyzone/index.php?id=247>).

For your information ethical approval is granted until **01 March 2013**. If you need approval beyond this point you will need to apply for an extension to approval at least two weeks prior to this explaining why the extension is needed, (please note however that a full re-application will not be necessary unless the protocol has changed). You should also note that if your approval is for one year, you will not be sent a reminder when it is due to lapse.

If you do not start the project within three months of this letter please contact the Research Ethics Office. Should you need to modify the project or request an extension to approval you will need approval for this and should follow the guidance relating to modifying approved applications: <http://www.kcl.ac.uk/research/ethics/applicants/modifications.html>

www.kcl.ac.uk

Appendix 4 –Ethical approvals

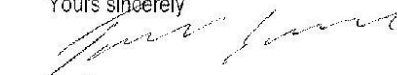
Any unforeseen ethical problems arising during the course of the project should be reported to the approving committee/panel. In the event of an untoward event or an adverse reaction a full report must be made to the Chairman of the approving committee/review panel within one week of the incident.

Please would you also note that we may, for the purposes of audit, contact you from time to time to ascertain the status of your research.

If you have any query about any aspect of this ethical approval, please contact your panel/committee administrator in the first instance (<http://www.kcl.ac.uk/research/ethics/contacts.html>). We wish you every success with this work.

With best wishes

Yours sincerely



Jim Summers
Senior Research Ethics Officer

Ethical approval from KEMRI for qualitative data collection



KENYA MEDICAL RESEARCH INSTITUTE

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KEMRI/RES/7/3/1

May 4, 2012

**TO: DR. RICHARD HARDING (PRINCIPAL INVESTIGATOR)
SCHOOL OF MEDICINE AT GUY'S KING'S COLLEGE AND
ST. THOMAS' HOSPITALS,
DEPARTMENT OF PALLIATIVE CARE, POLICY & REHABILITATION,
UK**

**ATT: DR. ZIPPORAH ALI,
NATIONAL COORDINATOR,
KENYA HOSPICES AND PALLIATIVE CARE ASSOCIATION**

Dear Sir,

**RE: NON-SSC PROTOCOL No. 274 (RE-SUBMISSION: REQUEST FOR
AMENDMENT 1): TREATMENT OUTCOMES IN PALLIATIVE CARE: A
RANDOMIZED CONTROLLED TRIAL**

The ERC Secretariat acknowledges receipt of your response letter and the amended version of the English Consent document on May 2, 2012.

This is to inform you that the Committee is satisfied that the issues raised at the 200th meeting of 17th April 2012 have been adequately addressed. You are therefore authorized to implement the change accordingly.

Please note that you are required to submit any further proposed revisions to the approved version of the protocol and consent forms to the SSC and ERC for review and approval prior to initiation. Any unanticipated problems that may arise during the conduct of the study must be reported to the ERC.

Sincerely,

**DR. CHRISTINE WASUNNA,
ACTING SECRETARY,
KEMRI ETHICS REVIEW COMMITTEE**

Ethical approval from Kings College for qualitative data collection

**Research Ethics
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Keira Lowther
Cicely Saunders Institute
Department of Palliative Care, Policy & Rehabilitation
King's College London
Bessmer Road
London SE5 9PJ

29 February 2012

Dear Keira

BDM/10/11-31 TOPCare: Treatment and Outcomes in Palliative Care: A randomised controlled trial.

Thank you for submitting a modification request for the above study. I am writing to confirm approval of this with the following provisos:

1. Previous participants who withdrew from the project should not be re-contacted for participation in the qualitative element of the study.
2. Consent Form: Please add a bullet point and tick box allowing participants to consent to being audio recorded.

The modification is summarised below:

1. Qualitative interviews will be conducted with participants to cover their experience of care in more depth.

If you have any queries regarding this application please contact the Research Ethics Office.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Catherine Fieulleau', written over a circular stamp or seal.

Catherine Fieulleau
Senior Research Ethics Officer

www.kcl.ac.uk

Appendix 5 - TOPCare protocol paper

Lowther et al. *BMC Infectious Diseases* 2012, **12**:288
http://www.biomedcentral.com/1471-2334/12/288



STUDY PROTOCOL

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Treatment outcomes in palliative care: the TOPCare study. A mixed methods phase III randomised controlled trial to assess the effectiveness of a nurse-led palliative care intervention for HIV positive patients on antiretroviral therapy

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Abstract

Background: Patients with HIV/AIDS on Antiretroviral Therapy (ART) suffer from physical, psychological and spiritual problems. Despite international policy explicitly stating that a multidimensional approach such as palliative care should be delivered throughout the disease trajectory and alongside treatment, the effectiveness of this approach has not been tested in ART-experienced populations.

Methods/design: This mixed methods study uses a Randomised Controlled Trial (RCT) to test the null hypothesis that receipt of palliative care in addition to standard HIV care does not affect pain compared to standard care alone. An additional qualitative component will explore the mechanism of action and participant experience. The sample size is designed to detect a statistically significant decrease in reported pain, determined by a two tailed test and a p value of ≤ 0.05 . Recruited patients will be adults on ART for more than one month, who report significant pain or symptoms which have lasted for more than two weeks (as measured by the African Palliative Care Association (APCA) African Palliative Outcome Scale (POS)). The intervention under trial is palliative care delivered by an existing HIV facility nurse trained to a set standard. Following an initial pilot the study will be delivered in two African countries, using two parallel independent Phase III clinical RCTs. Qualitative data will be collected from semi structured interviews and documentation from clinical encounters, to explore the experience of receiving palliative care in this context.

Discussion: The data provided by this study will provide evidence to inform the improvement of outcomes for people living with HIV and on ART in Africa.
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Keywords: HIV, ART, Palliative care, Africa, Evaluation

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Background

In 2009, the global number of people with HIV was 33.3 million (95% CI 31.4 million- 35.3 million) with the majority in sub Saharan Africa, where 22.5 million adults and children live with HIV infection [1]. Improved treatment and care programs are urgently required [2]. Despite recent treatment guideline changes, which have raised the recommended CD4 threshold for initiation of antiretroviral therapy (ART) [3] (indicating that the population of ART patients should be expected to increase), the World Health Organization (WHO) reports that the number of eligible patients receiving treatment has increased from 28% in 2008 to 36% in 2009 worldwide. Under the previous treatment guidelines, this proportion would have been 52% in 2009 [4]. This increase in the number of eligible patients will become a mounting clinical challenge.

Studies in Brazil [5], Malawi [6], USA [7], UK [8] and South Africa [9] demonstrate that people living with HIV continue to experience a significant symptom burden after ART initiation. This was clearly demonstrated by a large UK study of HIV outpatients [10], who reported physical, psychological and global distress and symptom counts which remained unaffected by treatment status, suggesting that accessing effective treatment for the virus might not be sufficient to alleviate suffering. The prevalence of symptoms and associated distress in this patient group can be caused by toxicities from the ART itself [11-13], symptoms of opportunistic infections and co-morbidities or HIV disease [7,10,14]. People with HIV report lower quality of life [6,15-17], attributed to their physical and psychological symptom burden. In Australia, patients with HIV receiving ART had a significantly higher prevalence of depression when compared with HIV negative patients recruited from the same clinics [18]. Data from a UK study confirm this, with psychological distress reported by 75% of a sample of HIV outpatients, regardless of treatment status [8]. In Sweden, although physical health status improved after ART initiation, patients reported a deterioration in emotional quality of life, associated with an increase in the number of adverse reactions they experienced [19]. In Tanzania 53% of patients attending a clinic (of whom the majority were receiving ART), had palliative care needs [20].

Palliative care is defined by the WHO [21] as an essential component of care for people living with HIV. Palliative care includes the assessment and treatment of pain and other symptoms, whether physical, psychosocial or spiritual in nature, delivered alongside treatment. Leading experts have highlighted the false dichotomy of palliative care treatment versus cure, particularly among the vulnerable poor in developing countries [22-27]. The WHO clearly identifies an urgent need for holistic

palliative care integrated with treatment for those suffering from chronic diseases such as HIV. This has been reiterated by UNAIDS, which has identified the misconception that palliative care is only appropriate for patients at the end of life, and is therefore working towards the availability of palliative care for all people living with HIV [28].

The WHO public health model of palliative care, developed in 1990, integrates palliative care into all of society, from community level to expert palliative care provision and in existing healthcare structures [29]. However, the pioneering service provision attempts and advocacy for this model are hampered by a lack of experimental research, and a lack of standardised measures and protocols, which would facilitate a more robust approach to healthcare evaluation and delivery [30]. For successful implementation, the WHO public health model of palliative care needs robust evidence of effectiveness in relevant contexts.

There are wider reasons beyond patient quality of life that indicate the importance of attention to palliative care-related problems. Depression and treatment of side effects are associated with non-adherence to ART [31,32], which increases viral resistance, rebound and infectiousness [33]. A recent systematic review of palliative care-related problems at HIV diagnosis identified significant physical and psychological symptoms among newly diagnosed HIV positive patients [34]. A systematic review of the evidence for effectiveness of HIV palliative care found that it improves anxiety, pain, symptoms, and insight but that the evidence was generated almost exclusively in the pre-ART era and in high income countries [24]. There are currently no known trials of palliative care for patients with HIV on ART. This lack of evidence originating from low and middle-income countries is problematic in light of the great disease burden in these areas.

We therefore aim to inform HIV service provision by conducting a randomised controlled trial (RCT) to assess the effectiveness of palliative care for HIV outpatients on ART, and present here the protocol for the phase III RCT with a qualitative component.

Methods/design

Aim and objectives

Aim

We aim to evaluate the efficacy, in terms of reported pain of a nurse led palliative care intervention for HIV patients on ART. Nurses will receive two weeks in depth training in palliative care and support and supervision from an experienced palliative care mentor. Two trials are being conducted, one in Mombasa, a low-income setting, and one in Cape Town, a middle-income setting. In line with guidance from the Medical Research

Council (MRC) on the evaluation of complex interventions, qualitative data will also be collected to complement the quantitative data and address the question of how the intervention might work [35].

Objectives

1. To investigate whether self-report pain and symptoms significantly improve for HIV positive patients under palliative care compared to those in standard HIV care.
2. To compare self-report adherence to ART under palliative care compared to standard HIV care.
3. To compare self-report health-related quality of life under palliative care compared to standard HIV care.
4. To compare additional multidimensional palliative care outcomes (psychological, social and spiritual wellbeing) under palliative care compared to standard HIV care.
5. To understand the process of receiving palliative care and identify any specific component which may be the most effective aspect (i.e. access to strong analgesia, multidimensional assessment, access to multidisciplinary team).

Study design

The study will consist of two fully powered, independent phase III clinical RCT's preceded by a pilot. Each trial will be powered and conducted in parallel to a common research design protocol, thus providing evidence of outcomes in two different settings.

Patients will be randomly allocated to standard HIV care or standard HIV care plus palliative care. The palliative care will be delivered within the existing HIV clinic, and by existing staff, using an integrated model, with the option to refer to a specialist palliative care provider for complex cases. The study has been designed with measures to minimise potential contamination. Once the study nurses have been trained in palliative care, they will only see the patients allocated to the intervention, and will not be required to work in the main clinic until completion of the trial.

The design will be longitudinal, using repeated measures. Patient-centred outcomes will be measured using quantitative questionnaires.

Outcomes

The primary outcome is self-reported pain after four months. The secondary outcomes are health-related quality of life; adherence to treatment; risk behaviours; and psychological morbidity and the core domains of palliative care as defined by the WHO (physical, psychological, social and spiritual well-being) as measured by the APCA African POS.

Patients will be followed up for four months and most outcomes are measured at baseline and monthly intervals, described below.

Control

Patients randomly allocated to the control arm will receive the usual clinical care delivered by the HIV clinic. Nurses who have had no exposure to palliative care will provide this service.

In Kenya this consists of six-monthly clinical assessments once ART has been established, with investigations and treatment for any relevant symptoms or problems. Patient may attend the clinic for medications refill only or may request more frequent appointments if they experience a problem. In South Africa, patients attend the public hospital monthly for a brief appointment to refill medications. They may present for additional appointments as necessary.

Intervention

Patients randomly allocated to the intervention arm will receive clinical care from a nurse who has received two weeks' training in palliative care and ongoing clinical support and supervision from experienced palliative care providers. The palliative care trained nurse will also have the option to refer complex cases for management at a hospice.

Minimum package of palliative care

Patients allocated to the intervention arm will receive an initial clinical assessment, followed by either one further visit or phone call within the first week, one further visit or phone call within the second week and one visit per month thereafter. The focus of the care provided will be on holistic assessment and management of physical, psychological, spiritual and social problems. This minimum package of care can be supplemented by additional clinical support as required on a case-by-case basis.

Intervention nurse training

Training will be provided by local expert palliative care sites, and will be delivered in an intensive 2-week period, tailored to the needs of patients living with HIV who are not necessarily in advanced stages and who are currently on ART.

The training will be designed using national and international guidelines [36,37] to ensure that the nurses are prepared to address the specific palliative care dimensions and needs of those living with HIV and taking ART, with specific focus on the management of common HIV symptoms. Within these two weeks, the nurses will also gain clinical experience, working in a palliative care setting.

Standardised assessment form

Assessment and management of multidimensional problems is a central part of palliative care. The trained nurse will use a standardised assessment form, developed by the study team drawing on tools and models used in sub-Saharan Africa, to assess the domains of palliative care as defined by the WHO [21] and monitor adherence.

Clinical support

The nurse will receive weekly clinical support from an experienced palliative care provider, where all cases will be reviewed and decisions appraised. Drugs needed for the intervention group not stocked in the study site pharmacy will be dispensed by the supporting palliative care service.

Referral

As part of clinical support, referral to the hospice will be available for patients in the intervention arm whose needs are “complex” or apparently refractory and who require assessment or intervention from the palliative care specialist partner site. Criteria for referral will be established prior to the study launch, and recorded in the clinical documentation.

Sample size

We used the largest known dataset generated by the APCA African POS (detailed below) to derive expected levels of change used in the sample size calculation. The dataset consisted of baseline data from a longitudinal evaluation of care and support which recruited 1337 HIV patients in Uganda and Kenya [38]. Stata v10.0 was used for calculations.

Sample size was first calculated based on change in the pain item of the APCA African POS, as the primary outcome. A clinically significant change in an APCA African POS item is a change of 1 point so this is identified as the expected change [39]. We propose a sample size of 56 per arm to be able to demonstrate a difference between treatment conditions for pain, symptoms, and both physical and psychological dimensions of quality of life (the latter as a mediating variable in a model of adherence). The study will recruit 60 patients per arm (120 total in each country), allowing for 6% drop-out/attrition [40].

Settings

The two participating HIV care facilities (one in Kenya and one in South Africa) are highly experienced HIV and ART service providers, with proven longevity. The study site in Kenya is a private clinic funded by private donations in a deprived area of Mombasa. Regular appointments are made to see a nurse for a health check

and ART refill, with frequency dependant on adherence, opportunistic infections and CD4. Patients have access to a physician if referred by the triaging nurse, and good access to essential medicines. The South African study site is a government-run clinic in district township, south-east of Cape Town. Patients have monthly appointments for a health check and ART refill, and have similar access to clinic physicians as in Kenya – upon nurse referral. Access to essential medicines is mostly reliable, but is hampered by economic constraints necessitating short prescriptions. In both countries, the providers of the palliative care training and support are longstanding local experts. In Kenya, training was provided by Kenyan Hospice and Palliative Care Association (KEHPCA) with support from an expert from Coast Hospice in Mombasa. In South Africa, training was provided by Hospice Palliative Care Association (HPCA) and support was provided by an expert from Helderberg Hospice.

Recruitment and consent

Screening and recruitment Because of organisational and logistical differences between the two study sites, recruitment will be performed in a slightly different way, whilst maintaining the integrity of random sampling and respecting the logistical constraints, patient flow and unique pressures of each clinic.

In Kenya, the initial patient to be screened will be chosen randomly using the number allocated to them at registration that day, and a number selected from a random number table. Once the initial patient has been screened, patients will be screened consecutively. In South Africa patients are simply screened consecutively according to the order in which they present at the clinic.

Inclusion/exclusion criteria

In both countries, patients included in the study must be adult patients (i.e. aged 18 years or above), with known HIV infection who have been receiving ART for more than one month.

Patients meeting these criteria will be screened by a researcher, using first two items of the APCA African POS. If they report a score of 3, 4 or 5 on either (possible 0–5 score), they will be asked whether they have been experiencing the pain or symptoms for 2 weeks or longer. Patients who answer in the affirmative will be eligible for participation. This is in order to identify those with symptoms which suggest a chronic rather than acute problem. The researcher will then outline the study content and demands and ask whether they would like to consent to participate. This process will take place every day during the data collection period,

although the time of the day will vary randomly in order to collect a representative sample of the clinic population.

In Kenya, potential participants will be screened for eligibility from a list of all patients currently in the clinic, in the triage room of the comprehensive care unit, where all HIV positive patients are seen. In South Africa, all patients in the clinic are HIV positive and on ART, therefore the researcher will sit in the clinic room with the nurse and will screen each potential participant as they attend their appointment. All patients who are called to see the nurse will be screened consecutively and invited to consent if eligible.

In summary, to be eligible for participation, patients must have sufficient cognitive ability to answer the outcome tool questions using either verbal or hand responses (see data collection below), be receiving ART for at least one month (based on clinic records) and must report either pain or symptoms of 3, 4 or 5 on the APCA African POS (i.e. severe to overwhelming) for longer than two weeks. Exclusion criteria include pain and symptoms with a duration of less than 2 weeks, receiving ART for Prevention of Mother To Child Transmission (PMTCT) of HIV, or for some other reason not related to personal clinical need or if the patient does not speak either English or Kiswahili in Kenya, and English, isiXhosa or Afrikaans in South Africa.

Consent

If eligible, the patient is taken through the information and consent sheet in a separate private space, respecting the patient flow of the clinic and the demands on patient time. Patients will have an information sheet read aloud to them, and will then be asked to sign or mark a consent form. All information and consent forms will be translated into the principal local languages. Consent using either a signature or mark will be obtained according to local custom or patient preference. All consent forms will be kept securely at the facility, and stored separately from outcome data. Each patient will be allocated a unique identifying number, kept by the researcher.

All participants will have the right to withdraw, without notice, at any point. Participants who withdraw from the intervention arm will continue to receive the intervention for the full four months. They will be asked whether they want their data to be withdrawn. If so, it will be deleted from the database and the paper copy will be destroyed. After quantitative data collection has finished, the dataset will be anonymised and from that point it will no longer be possible to identify individuals and withdraw data.

A record of the number of patients not agreeing to participate will be kept at each facility in accordance with CONSORT guidelines for the reporting of RCTs [41].

The sample for the qualitative interviews will be purposively drawn from intervention (n=20) and control patients (n=10) based on the clinical and demographic patient characteristics and results of the quantitative data collection i.e. psychological well-being. This will attempt to ensure a representative sample in terms of demographic and clinical data, and also in terms of psychological well-being and response to the intervention.

Randomisation

Consenting patients will be administered the initial assessment and subsequently randomised to intervention or control group. This is done using block randomisation to ensure a manageable work load for the nurse delivering the intervention, with 40 per block. Each study site has been issued with three sealable pots containing 20 pieces of paper with "I" for intervention and 20 pieces of paper with "C" for control. Once a piece of paper has been blindly selected by the researcher, the patients is informed whether they are in the control or intervention group and this is recorded on a form which is kept separately from the data collection tools and records. The piece of paper is discarded and the process continues until the pot is finished, when the next pot is then used. The allocation to control or intervention is not blinded as it would be impossible to maintain this blinding when the intervention was delivered.

Compensation

Study participants are not given financial compensation for their time, but they are given \$5USD towards transport expenses for data collection appointments. Transport for intervention patients clinical appointments (of which there are at least two more than research appointments) are not reimbursed as this may influence the outcome. For comfort, participants are given a drink and small snack on arrival for their data collection appointments.

Ethical considerations

Ethical approval has been sought and secured from Kings College London Research Ethics Committee (BDM/10/11-31), University of Cape Town (019/2011), Ministry of Health of the Western Cape (Research request ID: 10252) and Kenyan Medical Research Institute (KEMRI/RES/7/3/1).

A distress protocol will be used, with participants being offered the opportunity to cease the interview if they become distressed during questioning. They will be able to decide to restart or abandon the interview at their own discretion. All information gathered during data collection will be confidential, except in the situation of a participant or someone related to the participant being at

risk, in which case the information will be acted upon. Please see Figure 1 for study flow chart.

Data collection and analysis

Data will be collected by local researchers following the study protocol. They will be trained in quantitative and qualitative data collection methods, and will receive specific training for each tool used in this study.

Tools

The data collection tools are:

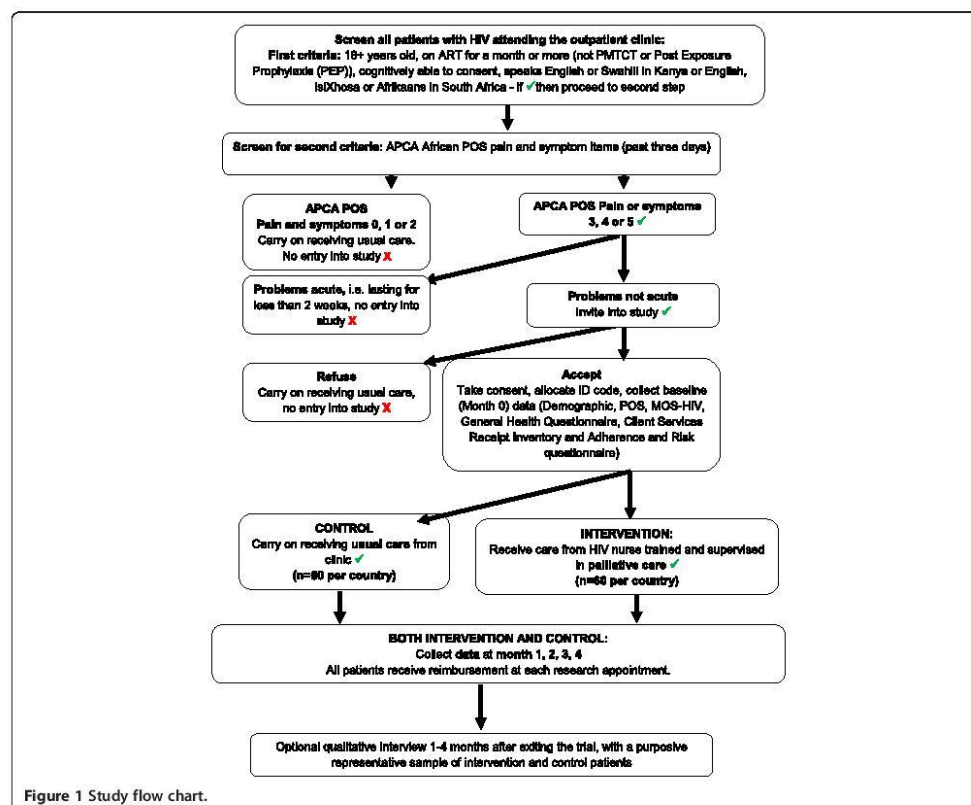
Patient demographic record

Administered once only, at month 0 This brief record will be used to record age, gender, couple status, number of children, number of financial dependents, education, recent CD4, date of ART initiation, WHO staging data and whether the patient is receiving TB treatment. This

questionnaire also includes assessment of relative socio-economic status, as used in the Demographic Health Surveys [42].

APCA AFRICAN POS (10 items)+ eastern Co-operative global performance scale (ECOG) (1 item)

Administered at months 0, 1, 2, 3 and 4 The original Palliative Outcome Scale (POS) was developed at King's College London [43,44] (further information and resources are available at <http://pos-pal.org/>). The APCA African POS was culturally adapted from the original POS during development in ten centres in six sub-Saharan African countries [45]. The ten items of the APCA African POS address the primary physical, emotional and spiritual concerns of patients and families with progressive disease using a scoring method appropriate for a range of literacy skills. Each item is scored on a scale of 0–5, and can be scored verbally or using



the “hand” method commonly used in Africa. Using this method, a closed fist represents “0”, moving up to an open hand scoring “5”. These methods have been validated among 300 patients under palliative care in Africa with a correlation of around 0.9 for verbal vs hand scoring methods for both pain scores and symptom scores. For those with no family carer, family items are scored as “0”, i.e. no problem [45]. The tool is sensitive to change and acceptable to patients, family and staff. Its brief nature makes it highly appropriate for use in a large-scale longitudinal study [46].

The ECOG is a single item measure of performance and is the most widely used performance measure [47]. Scores range from 0 (normal activity) to 4 (unable to get out of bed). It has been used in previous work amongst HIV positive people in Africa [48].

Medical outcome study -HIV (MOS-HIV quality of life measure)

Administered at months 0, 1, 2, 3 and 4 The MOS-HIV was originally developed as a general health questionnaire in the USA [49]. A modified HIV-specific version was developed and widely used. It has been culturally adapted to the Ugandan HIV setting [50] and has been used in Rwandan [51] Zimbabwean [52] and Ugandan populations [53]. The 35 items address the domains of role function, pain, physical functioning, cognitive functioning, social functioning, general health perception, mental health, health distress and vitality.

General health questionnaire-12 (GHQ)

Administered at months 0, 1, 2, 3 and 4 The GHQ-12 is a widely used measure of psychological morbidity [54]. It is the shortest validated version of the original GHQ, which was a 60-item instrument when it was first designed in the 1970s [55]. The GHQ-12 has been translated and validated into many languages including Kenyan Kiswahili [56].

Adherence and risk questionnaire

Administered at months 0, 2 and 4 only The adherence and risk questionnaire has been used for research in the UK, predominately with gay men [10,57]. The risk section of the questionnaire consists of three questions detailing sexual partners in the past four months, detailing unprotected sex and unprotected sex with people of unknown HIV status. The adherence questions ask participants how many ART doses they have missed in the past week.

Client services receipt inventory (CSRI)

Administered at months 0, 1, 2, 3 and 4 The CSRI aims to explore the components of care received by patients. The version of the CSRI used in this study is based was adapted from versions used in other palliative care research and adapted for use in Africa [58,59]. The version used for this study has been simplified in that instead of documenting time, the researcher records whether the client has received a service or not as a binary outcome.

Qualitative interview schedule

Administered for selected patients at month 4 The interview schedule was developed in collaboration with international researchers experienced in HIV and palliative care research and local researchers with an in depth knowledge of the delivery of palliative care at the study sites. It is designed to explore the intervention and control patients' perspectives on participating in a randomised trial, the intervention patients' experiences of receiving palliative care, and to determine the potential mechanism of action of the intervention.

Piloting

All tools were professionally translated into local languages and checked for consistency and accuracy by local researchers in each country and piloted with 35 patients in Kenya. This checked for clarity of questions, time required for data collection, patient burden and availability of requested information.

Quantitative data collection

Data collection will be conducted in the usual place of care, i.e. at home or at the clinic. For all tools, data will be collected as close as possible to the monthly timetable, with a two week grace period either side. Data collection appointments will be co-ordinated with clinical appointments where possible for minimal patient disruption.

Qualitative data collection

The qualitative data collection will be conducted between one and four months after quantitative data collection finishes, to minimise recall bias. Interviews will be digitally recorded and translated and transcribed by experienced local experts. Each transcription will be checked and validated by the researcher who conducted the interview.

Data management and quality assurance

A researcher will be employed at each participating centre. This person will be responsible for managing

recruitment, data collection and data entry. Fortnightly study team conference calls will be used to ensure that all queries are promptly resolved, attended by all members. All quantitative data will be double-entered into purpose designed EpiData databases. Discrepancies will be resolved by referring back to the original questionnaires.

Following data checking and cleaning, the data will be imported into Stata for analysis at KCL. Qualitative transcripts will be imported into NVivo (version 9) for analysis. All hard data will be stored for at least seven years in accordance with the UK Data Protection Act 1998.

Analysis

Quantitative analysis

Data will be described in two stages:

- 1) Cross sectional baseline analysis: descriptive analysis of demographic and clinical variables, baseline primary and secondary outcomes for the two groups (standard care and palliative care). Continuous variables will be presented as mean (standard deviation), median (range); categorical variables will be described as proportions. Baseline scores for primary and secondary outcome variables for two groups will be compared using two-sample t-test (or Mann–Whitney U test if non-normal distribution) for continuous data and Chi square test for categorical data.
- 2) Summary measures: change in primary and secondary outcomes from baseline to the final time point will be summarized, using paired t-tests or the non-parametric equivalent.

Longitudinal analysis will be performed to address the primary study objectives of comparing pain and other symptoms, (objective 1) and subsequently adherence (objective 2), health related quality of life (objective 3) and multidimensional palliative care outcomes such as psychological and spiritual well-being (objective 4), in the intervention and control groups. Factors of the APCA African POS were identified from APCA POS data from similar samples (high prevalence of HIV) in Sub Saharan Africa [60]. Three factors were identified which covered 1) physical and psychological symptoms, 2) interpersonal dimension and 3) the existential dimension. They will be analysed for differences between intervention and control groups. For continuous outcomes, the change in scores for two groups will be compared using general linear model with adjustment of baseline differences and covariates (demographics and clinical variables). For categorical outcomes, the two-group comparisons will be implemented using generalized linear model and adjusting for design effects, the repeated

measures will be taken into account using generalized estimating equations (GEE) technique.

The analysis will follow the principle of intention-to-treat. The p-values reported will be two-tailed and an alpha level of 0.05 will be used to assess statistical significance. The analysis will be carried out using non-missing data. The pattern of missing data and drop-outs will be investigated and sensitivity analysis will be performed to assess their impacts on outcomes. If the impact is great, a missing data strategy will be put in place using mean horizontal imputation and last value carried forward.

Further descriptive analysis will be conducted to determine the common features and differences between the three palliative care facilities, and the services received as recorded in the CSRI. Analysis of the CSRI will also allow us to determine a dosage effect for receipt of palliative care, as well as allow an evaluation of the palliative care received with respect to outcomes.

Qualitative analysis

Analysis of translated transcripts will be conducted using thematic content analysis [61]. The coding frame will be developed initially deductively, using themes from the topic guide, combined with inductive themes which emerge from the data, which will be generated iteratively as the analysis progresses. The coding will be conducted separately by two researchers, one from the study site and one from the UK, and then merged, to ensure a comprehensive and culturally sensitive framework.

The preliminary findings will be cross checked by the researcher based at the study site and presented to the study team in each country for proxy member checking to improve validity [62].

A model of the mechanism of the psychosocial aspect of palliative care will be constructed on the basis of the data if possible and relevant.

Dissemination

The audience for dissemination will include collaborating centres, participants, HIV clinicians, academic teaching staff in Africa, local community groups and non-governmental organisations, academic global research audiences, Ministries of Health and international non-governmental organisations.

Discussion

The data provided by this study will provide evidence to inform the provision of palliative care for people living with HIV and on ART, building on our previous work describing the palliative care problems of this group [8,10,24,46].

Aspects of this study are unique and will contribute to the body of knowledge. The choice of study design, the

first RCT in this field, will provide a clear answer to the question of whether palliative care for this group is effective and relevant. The multi-country aspect will illuminate the differences between low and middle income countries, and Southern and Eastern Africa, without inviting direct comparison of outcomes of two very different countries. Researchers in both countries will be locally recruited and trained by staff from King's College London, building local capacity. Steps have been taken to reduce potential bias, including using locally validated tools, which have been translated in all three study languages by experienced translators. Researchers have been trained on aspects of data collection, bias minimisation and potential sources of contamination and data will be double entered to avoid inaccuracies from human error.

The publication of this protocol presents increased transparency in the aims and objectives of the study and analysis of the generated data.

Abbreviations

APCA: African palliative care association; ART: Anti retroviral therapy; CSRI: Client services receipt inventory; ECOG: Eastern co-operative global performance scale; GHQ: General health questionnaire; HIV: Human immunodeficiency virus; HPCA: Hospice and palliative care association; KEHPCA: Kenyan hospice and palliative care association; MOS-HIV: Medical outcomes study HIV; MRC: Medical research council; PEP: Post exposure prophylaxis; PMTCT: Prevention of mother to child transmission; POS: Palliative outcomes scale; RCT: Randomised controlled trial; TB: Tuberculosis; WHO: World health organisation.

Competing interests

The authors declared that they have no competing interest.

Authors' contributions

RH and VS conceived of the original study with input from LS, LG, HK, AA, ZA, RJ and UH. LS, RH and VS drafted the manuscript with contributions from, LG, HK, AA, ZA, RJ and UH. All authors read and approved the final manuscript.

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Appendix 6 - Data collection tools

Demographic questionnaire

			ANSWER
D1	Gender	1=Male 2=Female	
D2	Age		
D3	Has a partner	1=Yes 2=No	
D4	How many people are you financially responsible for?		
D4a	How many children do you have?		
D5	What is the highest level of education you have attended?	0=No school 1 Four years of school or less 2=Primary 3=Secondary 4=Diploma 5=Degree or higher	
D6	Date enrolled in care at this facility		__/__/__
D7	Date of HIV diagnosis		__/__/__
D8	Date of ART initiation		__/__/__
D9	Most recent CD4 count		
D10	Date of most recent CD4 count		__/__/__
D11	WHO stage		
D12	Date of WHO stage recording		__/__/__
D13	Received AIDS diagnosis	1=Yes 2=No	
D14	Receiving TB treatment	1=Yes 2=No	
D14a	Does your immediate family know about your HIV status?	1=Yes 2=No	
D15	What is the main material used to make the floors of your house?	1=Earth, mud, sand 2=Cement 3=Linoleum 4=Parquet/polished wood 5=Tile 6=Carpet 7=Stone	
D16	What is the main material used to make the walls of your house?	0=Thatched/straw 1=Mud and poles 2=Un-burnt bricks 3=Burnt bricks with mud 4=Metal sheet 5=Cement blocks 6=Stone	

Appendix 6 – Data collection tools

		7=Wood timber 8=Burnt bricks with cement	
D17	What is the main material used to make the roof of your house?	1=Thatched 2=Wood/planks 3=Corrugated iron sheets 4=Asbestos 5=Tiles 6=Tin 7=Cement/concrete	
D18	What type of toilet do you use at home?	1=Private flush 2=Private VIP latrine 3=Private traditional pit (covered) 4=private traditional pit (uncovered) 5=public/shared 6=Bush/field/other	
D19	What is the main source of drinking water for your house?	0=Bottled 1=Piped inside house 2=Piped outside house (yard, public tap) 3=Protected well 4=Borehole 5=Spring/rain water 6=Unprotected well 7=River/stream/pond 8=Tanker truck	
D20	What type of fuel does your household mainly use for cooking?	0=Electricity 1=LPG/natural gas 2=Biogas 3=Paraffin/kerosene 4=Coal 5=Charcoal from wood 6=Firewood 7=Straw/shrubs/grass 8=Dung 9=No food cooked in household	
	Does anyone in the household own a...?		
D21	Bicycle	1=Yes 2=No	
D22	Refrigerator	1=Yes 2=No	
D23	Television	1=Yes 2=No	
D24	Car	1=Yes 2=No	
D25	Radio	1=Yes 2=No	

Appendix 6 – Data collection tools

The APOS & ECOG

	ASK THE PATIENT Questions 1-7	POSSIBLE RESPONSES	ANSWER
P1	Please rate your pain (from 0 = no pain to 5 = worst/overwhelming pain) during the last 3 days	0 = No pain at all 1 2 3 4 5 = Overwhelming. The worst pain you can imagine	
P2	Have any other symptoms (e.g. nausea, coughing or constipation) been affecting how you feel in the last 3 days?	0 = no, not at all 1 2 3 4 5 = overwhelmingly	
P3	Have you been feeling worried about your illness in the past 3 days?	0 = Not at all worried 1 2 3 4 5 = Worried all of the time	
P4	Over the past 3 days, have you been able to share how you are feeling with your family or friends?	0 = Not at all 1 2 3 4 5 = Yes, I've talked freely	
P5	Over the past 3 days have you felt that life was worthwhile?	0 = Not at all 1 2 3 4 5 = Yes, all the time	
P6	Over the past 3 days, have you felt at peace?	0 = Not at all 1 2 3 4 5 = Yes, all the time	
P7	Have you had enough help and advice for your family to plan for the future?	0 = None 1 2 3 4 5 = As much as wanted	
PE	ECOG Physical function of patient Rated by the interviewer	0= fully active, able to carry on all pre-disease performance without restriction 1=Restricted in physically strenuous activity but ambulatory and able to carry out light work, e.g., light house work, office work 2=Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours 3=Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours	

Appendix 6 – Data collection tools

		4=Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	
	Ask THE CARER Questions 8, 9 and 10 ONLY if consent given by patient and carer		
P8	How much information have you and your family been given?	0 = None 1 2 3 4 5 = As much as wanted 7 = N/A, no carer/consent not given 8 = Carer not present at time of interview	
P9	How confident does the family feel caring for ____?	0 = Not at all 1 2 3 4 5 = Very confident 7 = N/A, no carer/consent not given 8 = Carer not present at time of interview	
P10	Has the family been feeling worried about the patient over the last 3 days?	0 = Not at all worried 1 2 3 4 5 = Worried all of the time 7 = N/A, no carer/consent not given 8 = Carer not present at time of interview	

Appendix 6 – Data collection tools

The MOS-HIV

No.	QUESTION	POSSIBLE RESPONSES	ANSWER
<i>I would like to ask you a few questions about your health.</i>			
M1	In general would you say your health is:	1=Excellent 2=Very good 3=Good 4=Fair 5=Poor	
M2	How much <i>bodily</i> pain have you generally had during the past thirty days?	1=None 2=Very mild 3=Mild 4=Moderate 5=Severe 6=Very severe	
M3	During the past thirty days, how much did pain interfere with your normal work, including both work outside the home and housework?	1=Not at all 2=A little bit 3=Moderately 4=Quite a bit 5=Extremely	
<i>The following questions are about activities that a person might do during a typical day. Does your health now limit you in the following activities? And if so, how much?</i>			
		1=Yes, limited a lot 2=Yes, limited a little 3=No, not limited at all	
M4A	The kinds or amounts of vigorous activities you can do like digging, fetching water from a well, carrying a load, splitting firewood, running, lifting heavy objects or engaging in strenuous sports		
M4B	The kinds of moderate activities you can do like washing clothes, moving a jerrican of water or cleaning the house		
M4C	Walking up hill, climbing stairs		
M4D	Bending, lifting light objects or kneeling		
M4E	Walking a moderate distance, like the length of a football pitch or taking a village walk		
M4F	Feeding, dressing or bathing yourself or ability to use the latrine		
<i>The following questions are about work. Does your health now restrict you in doing the following kinds of work?</i>			
M5	Does your health keep you from working at a job, doing work around the house or attending school?	1=Yes 2=No	
M6	Have you been unable to do certain kinds or amounts of work, housework, schoolwork, because of your health?	1=Yes 2=No	
For each of the following questions, please tell me the answer that comes closest to the way you have been feeling.			
	(Interviewer must begin by reading this introductory question to the patient) How much of the time during the past 30 days:	1=All of the time 2=Most of the time 3=A good bit of the time 4=Some of the time 5=A little of the time	

Appendix 6 – Data collection tools

		6=None of the time	
M7	Has your health limited your social activities, like visiting with friends or family?		
M8A	Have you been a very nervous person?		
M8B	Have you felt calm and peaceful?		
M8C	Have you felt depressed?		
M8D	Have you been a happy person?		
M8E	Have you felt so depressed that nothing could cheer you up?		
M9A	Did you feel full of life and energy?		
M9B	Did you feel totally without energy?		
M9C	Did you feel tired?		
M9D	Did you have enough energy to do the things you wanted to do?		
M9E	Did you feel weighed down by your health problems?		
M9F	Were you discouraged by your health problems?		
M9G	Did you feel despair over your health problems?		
M9H	Were you afraid because of your health?		
M10A	Did you have difficulty reasoning and making decisions, for example, making plans or learning new things?		
M10B	Did you forget things that happened recently, for example, where you put things or when you had appointments?		
M10C	Did you have trouble keeping your attention on any activity for long?		
M10D	Did you have difficulty doing activities involving concentration and thinking?		
	Please tell me the answer that comes closest to describing whether the following statement is true or false for you.	1=Definitely true 2=Mostly true 3=Don't know 4=Mostly false 5=Definitely false	
M11A	You are somewhat ill		
M11B	You are as healthy as any other person you know		
M11C	Your health is excellent		
M11D	You have been feeling bad recently		

Appendix 6 – Data collection tools

M12	How has the quality of your life been during the past thirty days? That is, how have things been going for you?	1=Very well, could hardly be better 2=Pretty good 3=Good and bad parts bout equal 4=Pretty bad 5=Very bad, could hardly be worse	
M13	How would you rate your physical health and emotional condition now compared to thirty days ago?	1=Much better 2=A little better 3=About the same 4=A little worse 5=Much worse	

Appendix 6 – Data collection tools

GHQ-12

	Have you recently...		ANSWER
G1	Been able to concentrate on whatever you are doing?	1=Better than usual 2=Same as usual 3=Less than usual 4=Much less than usual	
G2	Lost much sleep over worry?	1=Not at all 2=No more than usual 3=Rather more than usual 4=Much more than usual	
G3	Felt that you were playing a useful part in things?	1=More than usual 2=Same as usual 3=Less so than usual 4=Much less than usual	
G4	Felt capable of making decisions about things?	1=More so than usual 2=Same as usual 3=Less so than usual 4=Much less capable	
G5	Felt constantly under strain?	1=Not at all 2=No more than usual 3=Rather more than usual 4=Much more than usual	
G6	Felt you couldn't overcome your difficulties?	1=Not at all 2=No more than usual 3=Rather more than usual 4=Much more than usual	
G7	Been able to enjoy your normal day-to-day activities?	1=More so than usual 2=Same as usual 3=Less so than usual 4=Much less than usual	
G8	Been able to face up to your problems?	1=More so than usual 2=Same as usual 3=Less able than usual 4=Much less than usual	
G9	Been feeling unhappy and depressed?	1=Not at all 2=No more than usual 3=Rather more than usual 4=Much more than usual	
G10	Been losing self-confidence in yourself?	1=Not at all 2=No more than usual 3=Rather more than usual 4=Much more than usual	
G11	Been thinking of yourself as a worthless person?	1=Not at all 2=No more than usual 3=Rather more than usual 4=Much more than usual	
G12	Been feeling reasonably happy, all things considered?	1=More so than usual 2=Same as usual 3=Less so than usual 4=Much less than usual	

Appendix 6 – Data collection tools

Adherence and risk

		Possible responses	ANSWER
R1	Have you had sex in the past two months?	1=Yes 2=No [go to question R4]	
R2	Have you had sex without protection in the past two months?	1=Yes 2=No [go to question R4] 9=Not applicable	
R3	Have you had sex without protection in the past four months, with a person whose status you did not know?	1=Yes 2=No 9=Not applicable	
R4	How many doses of ART have you missed in the past seven days?	Write the number. If none missed write 0 if don't know write 88	

Client services receipt inventory

	Area of care . In the past month have you received..?	8= Don't know	ANSWER
	SPIRITUAL		
C1	Visit by pastor/imam/ spiritual leader etc .	1=Yes 2=No	
C2	Discussion with clinic staff about spiritual worries	1=Yes 2=No	
C3	Prayer with staff	1=Yes 2=No	
	PSYCHOLOGICAL		
C4	Emotional support from staff	1=Yes 2=No	
C5	ART adherence counselling	1=Yes 2=No	
C6	Time to talk with staff about your worries. Have you felt listened to by staff?	1=Yes 2=No	
C7	Emotional support for your family	1=Yes 2=No	
	NURSING/MEDICAL		
C8	Discussion with nurse or doctor about your pain (NOT with me)	1=Yes 2=No	
C9	Any discussion about your physical symptoms (NOT with me)	1=Yes 2=No	
C10	Non-opioid (e.g. panado)	1=Yes 2=No	
C11	Weak opioid (e.g. something stronger than Panado)	1=Yes 2=No	
C12	Strong opioid (e.g. morphine)	1=Yes 2=No	
C13	Help with breathing problems	1=Yes 2=No	

Appendix 6 – Data collection tools

	Area of care . In the past month have you received..?	8= Don't know	ANSWER
C14	Medication to help with worrying/feeling sad or depressed	1=Yes 2=No	
C15	Medication for feeling sick or being sick	1=Yes 2=No	
C16	Medication for skin problems	1=Yes 2=No	
C17	Medication for diarrhoea	1=Yes 2=No	
C18	Medication for constipation	1=Yes 2=No	
	SOCIAL		
C19	Discussion with staff about your future if you were to get very sick	1=Yes 2=No	
C20	Planning ahead for your family if you were to get very sick	1=Yes 2=No	
C21	Nutritional support ie. Food baskets or parcels, supplements or rations	1=Yes 2=No	
C22	Financial support ie. Access or help with accessing funding or benefits, disability allowance, pension etc.	1=Yes 2=No	

Appendix 7 –Clinical assessment sheet

Patient's name _____ Date _____

PHYSICAL ASSESSMENT

Pain

Ask the patient to show where their pain comes on the scale of 0-5



Important questions to ask the patient

Where is the pain (there may be more than one pain)

When did it start?

What does it feel like? (eg. stabbing, cramping, burning etc)

Timing – is the pain there all the time or does it come and go?

Does the pain cause you to wake up at night?

Treatment – has any treatment been tried and has it helped?

Change – what makes it better or worse (eg movement, eating, time of day etc)?

Cause – what do you (the patient) think is causing the pain?

Pain assessment comments:

Body chart

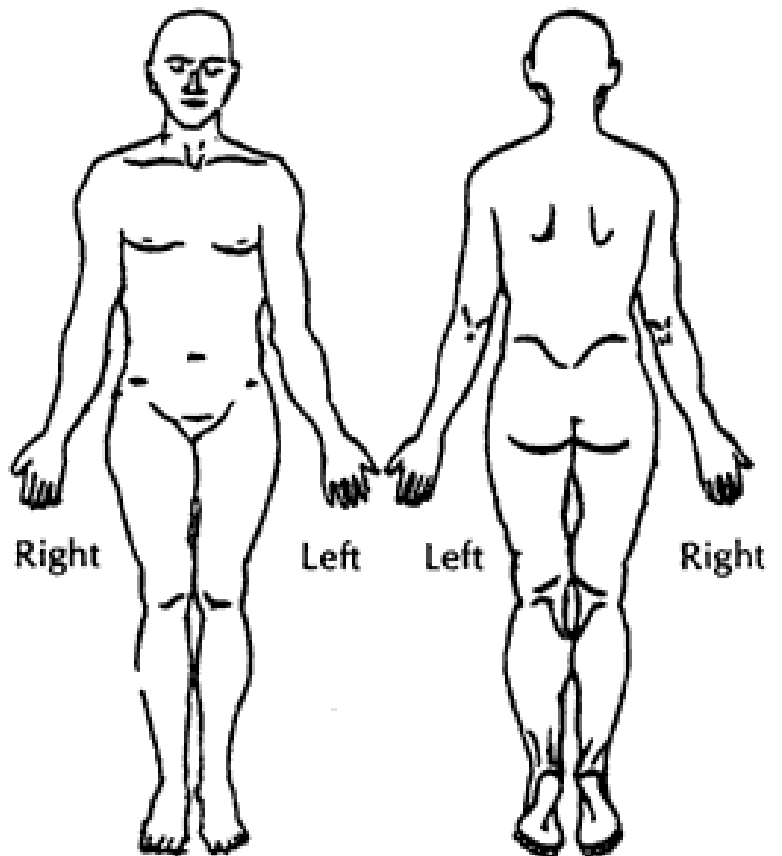
Mark on and describe sites of pain and symptoms

Include:

Chest

Abdomen

Neurological



Body chart assessment comments:

Could you list the five worst symptoms you have experienced in the past five days?

For example: nausea or vomiting, pain, lack of energy, lack of appetite, constipation, difficulty in sleeping, shortness of breath, dizziness. Difficulty seeing/hearing/moving/walking etc.

Activities of daily living

	Independent	Needs assistance	Dependent
Bathing			
Dressing			
Toilet			
Mobility			
Continence			
Feeding			

Activity of daily living assessment comments:

PSYCHOSOCIAL ASSESSMENT

Understanding of illness and consequences

What do you understand by your illness?

What does your family understand?

What is your main distress?

What is your family's main distress?

What are your expectations?

What are the family's expectations?

Appendix 7 –Clinical assessment sheet

Has the illness affected any close relationships? (this may include sexual issues)

What would help you to live well with your HIV and to be able to benefit from your treatment?

Understanding of illness assessment comments:

Family support (discuss)

Are they supportive?

▪ Are there any problems?

Financially

Emotionally

Socially

Spiritually

Family support assessment comments:

Economic situation (discuss)

Employment

Income

Accommodation

Medical aid

Insurance

Other expenses

Economic situation assessment comments:

Emotional assessment

Over the last two weeks have you been

bothered by:

little interest or pleasure in doing things

feeling depressed or hopeless

feeling sad

feeling worried

trouble falling asleep or sleeping too much

feeling tired or having little energy

poor appetite or overeating

feeling irritable

feeling bad about yourself – that you are a failure or have let yourself or your family down

trouble concentrating on things

moving or speaking so slowly other people could notice, or being very fidgety and

restless feeling nervous

thoughts that you would be better off dead or of hurting yourself in some way

If you have been bothered by any of these problems, how difficult have they made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all

Somewhat difficult

Very difficult

Extremely difficult

Emotional assessment comments:

SPIRITUAL ASSESSMENT

Discuss:

Faith – What do you believe has brought meaning to your life? Do you have a faith or belief?

Importance – How important is your faith or spirituality to you? How is it important?

Importance of religion/faith or belief system in life (please circle)

Great

Moderate

Unimportant

Nil

Community – Are you part of a religious or spiritual community? If you don't have a community, would it help you if you found one? Do you pray with others? Does it help you? Would you like to give us your religious adviser contact number so we can assist you in contacting them?

Peace - Are you at peace with your faith or belief? Are you at peace with your family?

Address or Application – Can we help in any way? How would you like me to address these issues in your healthcare? How do these issues impact your current situation? Do you have any fears or concerns regarding your spirituality which we may be able to address? Has your illness in any way affected your faith or belief? Would it help to see a pastor/imam/spiritual counsellor?

Spiritual assessment comments:

ANTI-RETROVIRAL THERAPY

Discuss:

Toleration

Adherence

Side effects

Other issues

Antiretroviral therapy assessment comments:

Summary

		Yes	No
1	Is the patient experiencing uncontrolled pain?		
2	Is the patient experiencing unresolved physical problems (including problems with sleeping, appetite, nausea, bowel, breathing or fatigue)?		
3	Does the patient have problems with daily living activities?		
4	Does the patient have any concerns about their understanding of their illness?		
5	Does the patient have problems with family relationships or support?		
6	Does the patient have financial or legal concerns that are causing distress or require assistance?		
7	Does the patient have psychological problems that are interfering with wellbeing or relationships?		
8	Does the patient have concerns about spiritual or existential issues?		
9	Does the patient have problems taking, tolerating, or adhering to ART?		

Appendix 8 - Ongoing record

Patient's name _____

Area	Problem	Action	Progress	Action
1 Pain	Date:	Date:	Date:	Date:
2 Physical	Date:	Date:	Date:	Date:
3 ADL	Date:	Date:	Date:	Date:
4 Understanding	Date:	Date:	Date:	Date:
5 Support	Date:	Date:	Date:	Date:
6 Finance	Date:	Date:	Date:	Date:
7 Psychological	Date:	Date:	Date:	Date:
8 Spiritual	Date:	Date:	Date:	Date:
9 ART	Date:	Date:	Date:	Date:
10 Other	Date:	Date:	Date:	Date:

Appendix 9 – Patient information and consent forms for phase 1 and 2

TOPCare trial Patient Information Sheet

REC Reference Number: BDM/10/11-13

You will be given a copy of this Information sheet

We would like to invite you to take part in this original research project. You should only participate if you want to; choosing not to take part will not disadvantage you in any way. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

We want to find out whether providing extra care and support makes people with HIV feel better if they are taking antiretroviral therapy (anti-HIV drugs, also known as ART). It is called the TOPcare Trial, standing for 'Treatment and Outcomes in Palliative care'.

Why have I been chosen?

We are asking every patient to take part who is aged over 18, has HIV, is taking antiretroviral therapy, and has severe pain or symptoms. We hope for 120 people at this facility to take part. You were chosen because you told the triage nurse that you had pain or symptoms which were severe or worse.

Do I have to take part?

No, you don't have to take part. You are free to withdraw at any time, and you don't have to give a reason. If you are one of the people chosen to receive care and support and you decide to withdraw from the study, you will still have the care and support for all the time you would have been in the study. You can also decide to remove all data about you from the study, up until July 2012. After that time it will no longer be possible to identify which data is yours.

What will happen if I take part?

You will be given this information to keep if you wish and asked to sign a consent form to show that you have agreed to participate. The research assistant will ask you to complete seven questionnaires, which will take about 40 minutes altogether. Then you will be asked to take a piece

of paper from a bag which will indicate whether you are going to receive ordinary care or extra care and support. Half the people in the study will get extra care and you have exactly the same chance as everyone else.

If you are in the ordinary care group, you will be asked to complete five or six questionnaires each month for four months with the research assistant, which will take about 30 minutes. Your care will be exactly the same as the normal care provided at the clinic. If you are in the extra care and support group, you will be assigned to a new nurse who has training in extra care and support. You will also be asked to complete the same five or six questionnaires once a month for four months with the research assistant. After four months the research will be over and you will continue to receive the standard care offered at this clinic.

The questionnaires are about how you feel and what care you have had. Some of the topics are

Physical problems like pain or symptoms

Whether you are worried

Whether you have problems working

Whether you feel happy or unhappy

What kinds of care you have received from the clinic

While taking part, there is a slight risk you may get anxious or embarrassed. You can ask to take a break or withdraw from the study at any time. Everything you say will be completely private unless the interviewer thinks you or your family's safety is at risk, in which case they may have to tell your care team.

Are there any other effects of being in the study?

If you choose to participate, we will provide US \$5 to pay for your transport to get to the facility. When we finish the study, we will give copies of the final report to the facility and arrange that you can have a copy if you want. If we find that extra care and support does help people taking ART, then we will provide training for all the nurses at this clinic, so that all the patients will be able to get extra care and support. This will happen after the end of the study.

Will my taking part in this study be kept confidential?

All the information which we collect during the interview will be kept strictly confidential and anonymous. You will not be identified in any way, and your personal details (for example name and address) will be kept separately from the information you give. We will NOT let anyone have any information that could identify you. Any information you give us will NOT be kept with anything that could identify you (like your name or address). You may withdraw your data from the project at any time up until July 2012.

What happens to the results of the research study?

We will add your results with those from 119 other people at this facility to find out whether people receiving extra care and support have better outcomes over time. We may also share the anonymous data with other researchers.

Who is organising the research?

This study is being organised by King's College London (UK). The Kenyan and King's College London Research Ethics Committees have reviewed this study and approved it for your protection.

Who can I contact?

If you'd like to talk to someone about the study, or get more information, or if you have experienced any harm as a result of this study, please contact:

Dr Richard Harding (Principal Investigator)

Department of Palliative Care, Policy and Rehabilitation

Cicely Saunders Institute, Kings College London

School of Medicine at Guy's, Kings and St Thomas Hospitals

Bessemer Road, London UK, SE5 9RJ

Tel: +44 (0) 20 7848 5518

Dr Zipporah Ali (Country Study Coordinator)

National Coordinator, Kenya Hospices and Palliative Care Association

Chaka Court, Off Argwings Kodhek Road, Next to Chaka PLACE, Hurlingham

P.O Box 20854-00202, Nairobi, Kenya

Tel: +254 (20) 2729302

Consent Form

REC Reference Number: BDM/10/11-13

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You may take a copy of this Consent Form to keep and refer to at any time

Please tick

I consent to the processing of my personal information for the purposes explained to me. I

understand that such information will be treated as strictly confidential and will be handled in accordance with the terms of the UK Data Protection Act 1998.

☐

I understand that if I decide at any time during the research that I no longer wish to participate in this project, I can notify the researchers involved and withdraw from it immediately without giving any reason. Furthermore, I understand that I will be able to withdraw my data at any time up to July 2012

☐

I agree that the research team or other researchers may use my data for future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. (In such cases, as with this project, data would not be identifiable in any report).

☐

Participant's Statement:

I _____ (*Participant's name*) agree that the research project named above has been explained to me to my satisfaction and I agree to take part in the study. I have read both the notes written above and the Information Sheet about the project, and understand what the research study involves.

Signed _____ Date _____ Researcher's signature here indicates
witness to thumbprint

Researcher's Statement:

I _____ confirm that I have carefully explained the nature, demands and any foreseeable risks (where applicable) of the proposed research to the participant.

Signed _____ Date _____

Patient Information Sheet for qualitative interview

You will be given a copy of this Information sheet

As a patient who has participated in the TOPCare study, we would like to invite you to take part in one extra interview. You should only participate if you want to; choosing not to take part will not disadvantage you in any way. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

We want to find out about your experience of receiving care in this study, and whether it has had any impact on your life, your relationships, your family or your own wellbeing. We will use this information to plan care for this clinic and others like it.

Why have I been chosen?

We are asking patients who have completed the TOPCare study. We hope for 25 people at this facility to agree to participate in this extra section.

Do I have to take part?

No, you don't have to take part. You are free to withdraw at any time, and you don't have to give a reason. You will continue to receive treatment at your clinic either way.

What will happen if I take part?

You will be given this information to keep if you wish and asked to sign a consent form to show that you have agreed to participate. The research assistant will ask you some questions about your experience of receiving care while you have been part of this study. This interview will take from 15 minutes to an hour, depending on how much you have to say. The interview will be recorded with your permission. None of the people providing you with care will hear the recording, just the research staff. Your personal details (e.g. name and address) will not be given to anyone and your answers will be kept separately. We will use all responses to write up reports on how we think receiving care affects people and what is the most important part of this care. Nothing you say will be identified as coming from you

You will be asked to do this interview ONCE.

While taking part, there is a slight risk you may be asked about things that could make you feel anxious or embarrassed. You can ask to take a break or stop the interview at any time. Everything you say will be completely private and confidential unless the interviewer thinks you or your family's safety is at risk. If this happens, they may have to tell someone in your care team who can ensure safety. This will not be done without discussing it with you first.

Are there any other effects of being in the study?

If you choose to participate, we will provide US \$5 to pay for your transport to get to the facility. When we finish the study, we will give copies of the final report to the facility and arrange that you can have a copy if you want. You will also be informed about a meeting where you will have an opportunity to hear about the findings of the study and ask questions of the research team in person.

Will my taking part in this study be kept confidential?

All the information which we collect during the interview will be kept strictly confidential and anonymous. You will not be identified in any way, and your personal details (for example name and address) will be kept separately from the information you give. We will NOT let anyone have any information that could identify you. Any information you give us will NOT be kept with anything that could identify you (like your name or address). You may withdraw your data from the project at any time up until December 2012.

What happens to the results of the research study?

The findings from the study will go together with the findings from the larger trial that you were also part of. This will help us to understand if people receiving extra care and support have better outcomes over time and what this experience is like. It will help people to understand what works in terms of care and why. We may also share the anonymous data with other researchers.

Who is organising the research?

This study is being organised by King's College London (UK). The Kenyan Medical Research Institute and King's College London Research Ethics Committees have reviewed this study and approved it for your protection (BDM/10/11-31)

Who can I contact?

If you'd like to talk to someone about the study, or get more information, or if you have experienced any harm as a result of this study, please contact either of the following:

Dr Richard Harding (Principal Investigator)

Reader in Palliative Care

Department of Palliative Care, Policy and Rehabilitation

Cecily Saunders Institute

Kings College London

School of Medicine at Guy's, Kings and St Thomas Hospitals

Bessemer Road

London UK, SE5 9RJ

Tel: +44 (0) 20 7848 5518

Dr Zipporah Ali (Country Study Coordinator)

National Coordinator, Kenya Hospices and Palliative Care Association

Chaka Court, Off Argwings Kodhek Road, Next to Chaka PLACE, Hurlingham

P.O Box 20854-00202, Nairobi, Kenya

Tel: +254 (20) 2729302

The Secretary, (Country Ethics Committee)

National Ethics Review Committee, KEMRI

P.O Box 54840-00200, Nairobi, Kenya

Tel: +254 (020) 2713349/2722541

Consent Form for Qualitative Interview

REC Reference Number: BDM/10/11-13

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You may take a copy of this Consent Form to keep and refer to at any time

Please tick

I consent to the processing of my personal information for the purposes explained to me. I understand that such information will be treated as strictly confidential and will be handled in accordance with the terms of the UK Data Protection Act 1998.

☐

I understand that if I decide at any time during the research that I no longer wish to participate in this project, I can notify the researchers involved and withdraw from it immediately without giving any reason. Furthermore, I understand that I will be able to withdraw my data at any time up to December 2012

☐

I agree that the research team or other researchers may use my data for future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. (In such cases, as with this project, data would not be identifiable in any report).

☐

I consent to my data being used in education for teaching and training.

☐

I consent to audio recording of my interview for research purposes

☐

Participant's Statement:

I _____ (Participant's name) agree that the research project named above has been explained to me to my satisfaction and I agree to take part in the study. I have read both the notes written above and the Information Sheet about the project, and understand what the research study involves.

Signed _____ Date _____

Researcher's signature here indicates witness to thumbprint

Researcher's Statement:

Appendix 9 – Patient information and consent forms for phase 1 and 2

I _____ confirm that I have carefully explained the nature, demands and any foreseeable risks (where applicable) of the proposed research to the participant.

Signed _____ Date _____

Appendix 10 - Topic guides for qualitative data collection

Interview topic guide - Intervention patients

Introduce self again, welcome client and thank for taking part. Explain that this is an opportunity to explain what it was like being in the TOPCare trial in a freer way – your own experience, in your own words.

Admin: - Complete consent form, Add in ID number, ask about more questions.

Briefly recount TOPCare trial, MOS-HIV, asked questions about emotional and physical well-being.

Present trajectory for specific patient and discuss how it tracks psychological well being and distress throughout the duration of TOPCare trial. i.e. started well, things became difficult, life got easier, psychological well-being remained unchanged.

Trajectory

Briefly, and with reference to the trajectory, how do you remember your well-being, psychologically and socially:

At the start of the trial

During the trial

At the end

After receiving care back in the CCC for some time?

(If any changes reported)What do you think caused these changes?

Do you think that your journey whilst on the trial is reflected in the trajectory?

Before the trial

Before the study began, how would you describe your emotional and social well-being/state of mind? Talk to me about your emotional health, worries, depression, family relationships, community relations, spiritual well-being, adherence, sexual risk taking. How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

Before the study began, how would you describe your physical well-being? talk to me about your physical health, pain, symptoms. How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

Before the study began, how would you describe your spiritual well-being? Talk to me about your feelings of peace and how your health affected your ability to participate in an active spiritual life (attending church/mosque). How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

During the trial

During the trial, how would you describe your emotional wellbeing/state of mind? Talk to me about your emotional health, worries, depression, family relationships, community relations, spiritual well-being, adherence, sexual risk taking. How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

During the trial, how would you describe your physical well-being? Talk to me about your physical health, pain, symptoms. How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

During the trial, how would you describe your spiritual well-being? Talk to me about your feelings of peace and how your health affected your ability to participate in an active spiritual life (attending church/mosque). How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

What would happen during the time you spent with the nurse(s)?

What kind of questions?

What kinds of concerns were discussed?

What was important to you to discuss during this time?

Do you think you got better in any way from seeing the nurse in the study? How?

Did you get worse any way?

Was it different in any way to the usual care you get at the clinic?

How easy was it to answer all the questions from the researcher?

How did it make you feel, to answer all the questions from the researcher?

After the trial

After returning to the CCC and receiving care as before, do you think your experience of palliative care has affected you, or changed you in any way?

Talk to me about your physical, emotional and spiritual well-being, worries, depression, family relationships, community relations, spiritual well-being, adherence, sexual risk taking, pain, symptoms.

How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

If change reported: What was important in this change taking place? Why/how did it happen?

If no change reported: What do you think you need to be healthier or happier?

For you, what was the most important thing about being on the trial – if anything, what helped you the most? Is there anything that could have been done differently which would have helped you?

Is there anything else you would like to add or tell me about your experiences of taking part in this research?

Thinking back, when I very first invited you into the TOPCare study, why did you say yes?

Interview topic guide - Control patients

Introduce self again, welcome client and thank for taking part. Explain that this is an opportunity to explain what it was like being in the TOPCare trial in a freer way – your own experience, in your own words.

Admin: - Complete consent form, Add in ID number, ask about more questions.

Briefly recount TOPCare trial, MOS-HIV, asked questions about emotional and physical well-being.

Trajectory

Present trajectory for specific patient and discuss how it tracks psychological well being and distress throughout the duration of TOPCare trial. i.e. started well, things became difficult, life got easier, psychological well-being remained unchanged. Briefly, and with reference to the trajectory, how do you remember your well-being, psychologically and socially:

At the start of the trial

During the trial

At the end

(If any changes reported)What do you think caused these changes? Do you think that your journey whilst on the trial is reflected in the trajectory?

Before the study

Before the study began, how would you describe your emotional and social well-being/state of mind? Talk to me about your emotional health, worries, depression, family relationships, community relations, spiritual well-being, adherence, sexual risk taking. How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

Before the study began, how would you describe your physical well-being? Talk to me about your physical health, pain, symptoms. How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

Before the study began, how would you describe your spiritual well-being? Talk to me about your feelings of peace and how your health affected your ability to participate in an active spiritual life (attending church/mosque). How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

During the trial

During the trial, how would you describe your emotional wellbeing/state of mind? Talk to me about your emotional health, worries, depression, family relationships, community relations, spiritual well-being, adherence, sexual risk taking. How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

During the trial, how would you describe your physical well-being? Talk to me about your physical health, pain, symptoms. How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

During the trial, how would you describe your spiritual well-being? Talk to me about your feelings of peace and how your health affected your ability to participate in an active spiritual life (attending church/mosque). How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

How easy was it to answer all the questions from the researcher?

How did it make you feel, to answer all the questions from the researcher?

After the trial

After finishing your time on the study, do you think your experience of being on the TOPCare trial has affected you, or changed you in any way?

Talk to me about your physical, emotional and spiritual well-being, worries, depression, family relationships, community relations, spiritual well-being, adherence, sexual risk taking, pain, symptoms. How did this affect your ability to work, day to day life, and your ability to function to an acceptable level. Why was that?

If change reported: What was important in this change taking place? Why/how did it happen?

If no change reported: What do you think you need to be healthier or happier?

For you, what was the most important thing about being on the trial – if anything what helped you the most? Is there anything else you would like to add or tell me about your experiences of taking part in this research?

Thinking back, when I very first invited you into the TOPCare study, why did you say yes?

Prompts and probes

<p>Amplification:</p> <p>Could you tell me a little more about that? Could you give me an example of that? When you say that, what gave you that impression? What exactly was it that you liked? How did you respond when? What did you feel when? Why do you think this is important? What effect did that have on you? Did that help in any way?</p> <p>Explanatory:</p> <p>What makes you say that? What was it about this that made you feel/do/decide to etc.</p>	<p>Clarification:</p> <p>How was that helpful/unhelpful/important/ difficult? Could you explain what you mean by.....? Before you said..... but you also say[highlighting contradiction]. What are the main feelings you're left with?</p> <p>In-depth iterative probing:</p> <p>This may sound like an obvious question, but..... I want to make sure I've really understood you. What was it exactly that you meant by.....?</p>
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Appendix 11 - Confidential Disclosure Agreement for Transcription and translation services

This Agreement is entered into this 09 day of August, 2012 by and between xxxx (hereinafter "Recipient") and Keira Lowther, with offices at King's College London, London, UK (hereinafter "Discloser").

WHEREAS Discloser possesses certain ideas and information relating to patient and psychosocial care provider personal identity, demographic details and opinions of research participants that is confidential and proprietary to Discloser (hereinafter "Confidential Information"); and

WHEREAS the Recipient is willing to receive disclosure of the Confidential Information pursuant to the terms of this Agreement for the purpose of transcription and translation of audio interviews;

NOW THEREFORE, in consideration for the mutual undertakings of the Discloser and the Recipient under this Agreement, the parties agree as follows:

1. Disclosure. Discloser agrees to disclose, and Receiver agrees to receive the Confidential Information.

2. Confidentiality.

2.1 No Use. Recipient agrees not to use the Confidential Information in any way, except for the purpose set forth above.

2.2 No Disclosure. Recipient agrees to use its best efforts to prevent and protect the Confidential Information, or any part thereof, from disclosure to any person other than the Recipient.

2.3 Protection of Secrecy. Recipient agrees to take all steps reasonably necessary to protect the secrecy of the Confidential Information, and to prevent the Confidential Information from falling into the public domain or into the possession of unauthorized persons.

3. Limits on Confidential Information. Confidential Information shall not be deemed proprietary and the Recipient shall have no obligation with respect to such information where the information:

(a) was known to Recipient prior to receiving any of the Confidential Information from Discloser;

(b) has become publicly known through no wrongful act of Recipient;

(c) was received by Recipient without breach of this Agreement from a third party without restriction as to the use and disclosure of the information;

(d) was independently developed by Recipient without use of the Confidential Information; or

(e) was ordered to be publicly released by the requirement of a government agency.

4. Ownership of Confidential Information. Recipient agrees that all Confidential Information shall remain the property of Discloser, and that Discloser may use such Confidential Information for any

Appendix 11 –Confidential disclosure agreement for transcription and translation service

purpose without obligation to Recipient. Nothing contained herein shall be construed as granting or implying any transfer of rights to Recipient in the Confidential Information, or any patents or other intellectual property protecting or relating to the Confidential Information.

5. Term and Termination. The obligations of this Agreement shall be continuing until the Confidential Information disclosed to Recipient is no longer confidential.

6. Survival of Rights and Obligations. This Agreement shall be binding upon, inure to the benefit of, and be enforceable by (a) Discloser, its successors, and assigns; and (b) Recipient, its successors and assigns.

IN WITNESS WHEREOF, the parties have executed this agreement effective as of the date first written above.

DISCLOSER Keira Lowther

RECIPIENT

Signed:



Signed:

Print Name:

Print Name: KEIRA LOWTHER

Title:

Title: Ms

Date:

Date: 09 August 2012

Appendix 12 – Recruitment progress monitoring spreadsheet

Appendix 12 – Recruitment progress monitoring spreadsheet

Clipboard		Font		Alignment		Number		Styles									
I65		fx		120													
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q
1	Kenyan Recruitment Timeline																
2	Week	Data from end of week commencing	Total intervention patients		Total control patients		Total screened	Total patients meeting first criteria (HIV,ART,adult)	Total patients POS>or=3	Total meeting inclusion criteria	Total refused	Total consented/ enrolled	Total completed	% of total on ART and eligible for	Refusal rate	% of total screened meeting 1st criteria	% of those on ART eligible for
3			Actual	Cumulative	Actual	Cumulative								13.28%	53.58%	79.04%	17.26%
4	1	25.07.2011	0	0	4	4	40	28	6	6	2	4	0	15.00%	33.33%	70.00%	21.43%
5	2	1.08.2011	4	4	3	7	105	92	15	15	8	7	0	14.29%	53.33%	87.62%	16.30%
6	3	8.08.2011	5	9	3	10	78	70	10	10	2	8	0	12.82%	20.00%	89.74%	14.29%
7	4	15.08.2011	2	11	2	12	101	90	10	10	6	4	0	9.90%	60.00%	89.11%	11.11%
8	5	22.08.2011	3	14	4	16	62	54	8	8	1	7	0	12.90%	12.50%	87.10%	14.81%
9	6	29.08.2011	1	15	0	16	39	27	2	2	1	1	0	5.13%	50.00%	69.23%	7.41%
10	7	5.09.2011	0	15	1	17	30	11	4	4	3	1	0	13.33%	75.00%	36.67%	36.36%
11	8	12.09.2011	3	18	2	19	109	80	18	18	13	5	0	16.51%	72.22%	73.39%	22.50%
12	9	19.09.2011	3	21	1	20	96	74	11	11	7	4	0	11.46%	63.64%	77.08%	14.86%
13	10	26.09.2011	3	24	1	21	76	62	13	13	9	4	0	17.11%	69.23%	81.58%	20.97%
14	11	3.10.2011	3	27	2	23	97	82	14	14	9	5	0	14.43%	64.29%	84.54%	17.07%
15	12	10.10.2011	3	30	2	25	67	54	9	9	4	5	0	13.43%	44.44%	80.60%	16.67%
16	13	17.10.2011	2	32	3	28	94	67	12	12	7	5	0	12.77%	58.33%	71.28%	17.91%
17	14	24.10.2011	2	34	3	31	94	81	11	11	6	5	0	11.70%	54.55%	86.17%	13.58%
18	15	31.10.2011	3	37	2	33	119	93	15	15	10	5	0	12.61%	66.67%	78.15%	16.13%
19	16	7.11.2011	1	38	2	35	69	57	7	7	4	3	0	10.14%	57.14%	82.61%	12.28%
20	17	14.11.2011	2	40	4	39	102	80	13	13	7	6	0	12.75%	53.85%	78.43%	16.25%
21	18	21.11.2011	2	42	1	40	34	28	5	5	2	3	5	14.71%	40.00%	82.35%	17.86%
22	19	28.11.2011	3	45	0	40	61	53	7	7	4	3	2	11.48%	57.14%	86.89%	13.21%
23	20	5.12.2011	0	45	0	40	0	0	0	0	0	0	5				
24	21	12.12.2011	0	45	0	40	0	0	0	0	0	0	6				
25	22	19.12.2011	0	45	0	40	0	0	0	0	0	0	3				
26	23	02.01.2012	0	45	0	40	0	0	0	0	0	0	1				
27	24	09.01.2012	4	49	2	42	126	102	13	13	7	6	5	10.32%	53.85%	80.95%	12.75%
28	25	16.01.2012	3	52	2	44	93	77	16	16	11	5	6	17.20%	68.75%	82.80%	20.78%
29	26	23.01.2012	4	56	1	45	89	68	11	11	6	5	0	12.36%	54.55%	76.40%	16.18%
30	27	30.01.2012	2	58	3	48	74	62	11	11	6	5	1	14.86%	54.55%	83.78%	17.74%
31	28	06.02.2012	2	60	2	50	85	70	11	11	7	4	10	12.94%	63.64%	82.35%	15.71%
32	29	13.02.2012	0	60	4	54	46	36	7	7	3	4	7	15.22%	42.86%	78.26%	19.44%
33	30	20.02.2012	0	60	4	58	61	48	7	7	3	4	6	11.48%	42.86%	78.69%	14.58%
34	31	27.02.2012	0	60	2	60	23	18	5	5	3	2	1	21.74%	60.00%	78.26%	27.78%
35	32	05.03.2012		60		60							9				
36	33	12.03.2012		60		60							5				
37	34	19.03.2012		60		60							1				
38	35	26.03.2012		60		60							1				
39	36	02.04.2012		60		60							1				
40	37	09.04.2012		60		60							0				

Appendix 13 – Extract of Project Journal

30/07/2013 14:05

All the data is coded into nodes and the intervention interviews are all checked.

Hypotheses at the moment are that a sense of well-being may lead to a sense of social value, which could facilitate the rejection or active resistance to stigma messages? The original deductive codes of Physical, social, psychological and spiritual have been developed to include topics which arose inductively such as disclosure, compassion, identity, hope, and concepts of attribution of improvement and content of the intervention: health education counselling and medication management.

Rather than divide up the symptoms and complaints into specific psychological or physical symptoms, although these are sometimes decided to be relevant, it was more pertinent to differentiate whether these symptoms were problematic or not. Psychological symptoms such as fear, shame, sadness and anxiety were also fine grain coded when more detail was provided by participants.

Main themes at this moment appear to be: The therapeutic value of talking process, Stigma, Identity, Fear, Well-being or normality,

I think these all need to be addressed in order to heal or become "normal" as defined by the participants - these are the active ingredients. Talking and connecting with team led to increase in social value and reparation of identity, and ability to fulfil social role such as breadwinning or caretaking.

Fear was addressed by acceptance and non judgementalism from the study team and through health education. Created a tentative model for the resistance to stigma based on Goudge et al

09/08/2013 11:41

Following a meeting with RH, I have revised the coding framework to make it more conceptualised and clearer for someone external to look at.

Is this a barrier to clear transparent analysis? Process towards developing concepts within the data.

I have developed the code "coping" to "Living with HIV". Do codes such as financial burden belong with this code - suggesting that living with HIV creates or exacerbates financial burden? This is not clear from the financial burden data. Do this population experience financial burden, regardless of HIV diagnosis.

Appendix 14 – Definition of themes and sub-themes in coding framework

Each theme and subtheme is listed in this appendix with a brief definition. They are presented alphabetically, with major themes in uppercase, and their sub-themes in sentence case.

Ability to self care: Descriptions of participants take care of themselves in terms of personal hygiene and maintenance

Acceptance of oneself and of status: Participants report of becoming more accepting of HIV positive diagnosis and self as a valid human being

Active ingredients of intervention: Aspect of the intervention which produces the therapeutic benefit

Active resistance: Response to hearing stigmatising messages or experiencing HIV-associated discrimination and actively resisting the stigma, through action or words

ART adherence: Reports of taking medication, difficulties taking medication or related information

ART adherence counselling: Descriptions of counselling given by study nurses to facilitate ART adherence

Being known: Participants descriptions of benefits of feeling known by the study team, and the effects that this had on their mental health and well-being

Being listened to: Descriptions of the experience of being listened to and having someone to talk to

Blaming God: Reports of blaming God for their HIV positive diagnosis and the consequences

Care taking or bread winning: Descriptions of social roles within the household

Communication: Participant descriptions of the therapeutic benefits of effective communication during participation in the study.

Compassion for others: Participant descriptions of their compassion for other people, and acknowledgement of their suffering

Compassionate care: One of the therapeutic aspects of participation, describing the approach and supportive way the study team interacted with participants. Included the sub themes of being known and feeling treated well

Consent: Data concerning the consent process, informed consent and reasons why participants gave their consent to participate in the study.

Content of intervention: Descriptions of what happened during palliative care appointments with the study nurses, including counselling

Corporate religious practice: Participant descriptions of their participation in collective religious experiences such as attending church, choir, prayer meetings or other events.

Counselling: Reports of counselling as part descriptions of the content of the intervention

Counselling for emotional support: Specific reports of counselling which was perceived by participants as emotionally supportive, such as management of emotional and psychological pain

Counselling for social support: Specific reports of counselling which provided social support, such as guidance on how to manage relationships

Counselling for spiritual care: Participant descriptions of spiritual guidance and care provided by the study nurses, for example advising participants to attend church, or read the Bible, or praying with them

Disclosure event: Participants descriptions of how, when and why they disclosed their HIV positive status, and to who. This also included the decision making process of who to disclose to and why

Effective Counselling: Active ingredient of the intervention describing the experience and effect of receiving counselling which met participant need

Enacted stigma: Descriptions of participant experience of discrimination

Experience of healthcare: Participants' descriptions of healthcare beyond that received as part of the study, including government clinics and private healthcare

Experience of participation in research: Reports of the participants' experiences of being recruited in a study: relationships with researchers and study nurses and the research process

EXPERIENCE OF RESEARCH: Participant descriptions of their experiences of research, including consent, content of the intervention, participation and understanding of the research process

Fear: Participant descriptions of experiencing fear or worry

Fear for health: Participant report of fear for their future well-being, often whether they would be able to get better and resume their previous life

Fear of being unable to fulfil role: Data pertaining to the fear that the participant would not be able to care for their family or earn a living in the future, often due to poor health

Fear of death: Participant reports of uncertainty in their future, and their fears that they might die soon, and fear for the consequences of this.

Fear of disclosure: Social fear of discrimination or isolation related to disclosure of HIV status, both accidentally or inadvertently or on purpose.

Feeling treated well: A therapeutic aspect of participation concerning the feeling of being subject to good hospitality, or otherwise being treated well or nicely

Felt normative stigma: Participant descriptions of stigma which were accepted in their culture and community

Financial burden: Participants descriptions of the experience of feeling financial constraint, or burden and of being a burden to others.

Financial support: Descriptions of financial support as part of the content of the intervention for participants

Free from mental strain: Participants descriptions of being freed from their previous mental strain during participation in the trial, as a source of hope

Freedom: Participant report of the importance of freedom in communication, that it should be unrestrained for full benefit

Fulfilling role: Data describing participant social well-being in terms of their ability to fulfil their socially prescribed role

Good nutrition: Participant reports of the importance of good nutrition for positive physical well-being

Gratitude to God: Patient descriptions of their gratitude to God for their current state of health, or relationships or other aspects of their lives that they were happy with

Growth in hope: Sub theme of hope as a part of spiritual well-being, encompassing participant descriptions of what cause an increase in their feelings of hope

Health education: Data regarding information of health promoting nature, given to the participants

Hope: Participants description of hope or other aspirations for the future, as part of spiritual well-being, including descriptions of growth in hope and loss of hope

Identity: Participant descriptions of how they see themselves and aspects of their personhood and self-image

Increasing trust in HCP: Participants descriptions of increasing trust and the result of that trust in the therapeutic relationship with health care providers during receipt of the intervention

Individual religious practice: Descriptions of prayer and devotional activities practiced alone

Insight and understanding: An active ingredient of the intervention describing the effect of counselling and health education on mental health and well-being

Interaction with healthcare professionals outside of study: Descriptions of contact participants had with medical or nursing staff outside of the study, usually in the CC or other hospitals such as the Government hospital

Internalised stigma: Participants descriptions of negative feelings they had about themselves, which stemmed from the stigmatising view of their community, which they had internalised as their own, creating distress and inner conflict

Judgement or rejection by God: Participants description of rationalisations they made about how God might be feeling negatively about them, or their actions or the situation they found themselves in as a PLWH, sometimes associated with internalised stigma

Juice and biscuits: Data referring to the refreshments received by participants on arrival for an appointment

Lack of social support – isolation: Participants descriptions of being isolated from family or community, whether self imposed or as a result of discrimination

Light beyond being sick: Participants increase in hope due to decrease in symptoms and physical and psychological complaints. This refers to participants hope for the future, and the possibilities they believed were not available to them

LIVING WITH HIV: Major theme encompassing all data relevant to the experience of life with HIV

Long life: Participants descriptions of hoping for the future, and realising that they could live when previously they thought they would die imminently; a source of increasing hope.

Lost hope: Participant's descriptions of when they had experienced a decrease in hope

Material support: A therapeutic aspect of participation. Data describing the therapeutic benefit of receiving material support such as refreshments and cash, rather than emotional or social support

Medication: Participant descriptions of the therapeutic effect of appropriate medication – an active ingredient of the intervention

Medication management: Participants descriptive comments about medication as content of the intervention

Motivated by getting better: Participants accounts of feeling improved well-being due to previous improvements, which increased hope and motivation for future improvement

Negotiation of sex: Participants descriptions of how they negotiated sex and safer sex with their partners, as part of sexual well-being

No engagement with religious practice: Participant descriptions of not engaging with religious practice. Sometimes due to feeling rejected by God, or just because they were not interested in spirituality and religion

Nutrition counselling: Descriptions of content of the intervention regarding nutrition advice and diet counselling

Open communication: Descriptive accounts of the benefits of open communication as a therapeutic aspect of participation in the study

Patient perspective of intervention: Participants' view and opinions on the relevance, value and effect of the study on them

Peace: Descriptions of feeling at peace, in terms of inner peace, peace in relationships and feelings of reconciliation with others

Personal strength: Descriptions of inner strength and resolve, with increases associated with improvements in self image

Physical and psychological interaction: Descriptions of the effects of relief of physical symptoms on psychological symptoms and vice versa

Physical well-being: Descriptive accounts of physical well-being, including symptoms, and nutrition

Possibility to regain role: Data pertaining to social role fulfilment, and the hope participants express that they might earn money or take care of their family otherwise in the future

Praying for a cure: Descriptions of participants praying to God to cure them of HIV

Presence of social support: Participants descriptive accounts of the provision of social support from partners, families or those in their community.

PROMS as prompts: Participant reports if using the PROMs as a prompt to self care, either as reflective material or as an indication of a health promotion message.

Protected sex: Participants descriptions of negotiating, the importance of or whether they have protected sex with their partners

Psychological well-being: Data pertaining to psychological symptoms and alleviation of psychological symptoms

Rejection of sexuality or sexual practice: Participants decisions to not engage in sexual activity after their HIV positive diagnosis.

Relationship as source of distress: Accounts of intimate partner verbal, physical or emotional abuse, and how this distressed the participants

Relationship as source of support: Accounts of partners who were supportive toward the participant

Relationship counselling: Content of the intervention, descriptions of participants' receipt of relationship and couples counselling

Relief from financial burden: Data describing the therapeutic aspect of materials support specifically the therapeutic aspect of relief of financial constraint

Relief of physical symptoms: Reports of relief of physical symptoms such as pain, pruritis or numbness

Relief of psychological symptoms: Reports of relief of psychological symptoms such as worry, fear or sadness

Religious practice: Descriptive accounts of prayer, attending church or mosque

Resistance to stigma: Participants descriptions of their internal or external resistant response to stigma

Resistant thinking: Internal mental rejection of stigmatising messages

Restoration: Participants descriptions of inner restoration of self-image or self perception which was restored to pre-HIV state

Role: Accounts of social role, fulfilling it, being unable to fulfil it, with associated distress

Sadness: Participants descriptions of feeling sad, depressed or in a low mood

Self determination: Participants accounts of feelings of empowerment or situations where they were able to control their lives in ways which they had not previously

Self image: Descriptive data of how participants saw themselves, and felt about themselves as human beings

Sex as therapy: Participants descriptions of using sex with their partners as a therapeutic act, which they described, relieved physical symptoms

Sexual health counselling: Descriptions of the content of the intervention including counselling on protected sex, and management of sexually transmitted infections

Sexual well-being: All participants reported data pertaining to participant's sexual health and well-being

Shame: Descriptions of feeling shame, or feeling shamed by others, usually due to inability to fulfil social role or HIV-related stigma

Social or emotional support from study team: Descriptions of participants' feelings of being supported by the study team

Social support: As part of social well-being, the extent to which participants describe feeling supported by their community or not.

Social support: Data attributing social support as a therapeutic aspect of participation, received from the study team religious communities or from peers.

Social support from peers: Participants descriptions of feeling supported through knowledge that they had peers, through contact with their peers, and the impact this had on participants

Social well-being: Descriptions of social support, social role and social shame

SOURCES OF BENEFIT: Theme containing data on active ingredients and therapeutic aspects of participation

Spiritual: Descriptive accounts of spiritual well-being, engagement with corporate or personal religious activity, and blaming God and receiving support from religious or spiritual practices

Stigma: participants Descriptions of experiencing stigma or discrimination through rejection, isolation or persecution

Strategic avoidance: Participants descriptions of resistance to stigma through avoiding confrontation or situations where they could reasonably expect to experience stigma or discrimination as a results of their HIV positive diagnosis

Stress or anxiety: Participants descriptions of feeling anxious or stressed as a psychological symptoms

Suicidal thoughts: Descriptions of suicidal thoughts, ideation and plans made by participants

Support from religious practice: Participants descriptions of the support they received from religious practice, either from the religious community or from the spiritual practices

Symptom burden: Sub theme of living with HIV encompassing physical, psychological, social spiritual and sexual well-being

Taking time: Participants accounts of the therapeutic effect of the study nurses taking time to talk during delivery of the intervention

Talking to share and relieve burdens: Data describing the therapeutic aspect of talking and communication and the psychological relief that sharing emotional burdens brought

Troubling physical symptoms: Participants accounts of persistent troubling physical symptoms

Troubling psychological symptoms: Participants accounts of persistent troubling psychological symptoms

Trust in God: Descriptions of participants trust in God, including trust for the future, resignation that this was God's plan, and fatalism and expressions of fluctuating trust.

Unable to fulfil role: Participant accounts of situations where they were unable to fulfil the role expected of them by their community, and the impact this had on their well-being and self-image.

Understanding of research process: Descriptive accounts of participants' perceptions and understandings of research processes, such as randomisation, consent, control group allocation and the approach of the researcher to data collection

Unprotected sex: Participants accounts of unprotected sex, negotiation and avoidance of unprotected sex and their knowledge of the associated risks

Waiting time: Participants descriptions of waiting to be seen for care in the standard care clinic, their feelings about this and the impact that this had on their well-being

Appendix 15 - Preliminary bivariate analysis to address objective 1

Data was analysed as per the analysis plan. To present the data and demonstrate the distribution of dependent variables, data have been modified to simplify analysis: age has been divided into decades, time since HIV positive diagnosis into years, and time on ART into years.

Table 0-1 Preliminary bivariate analysis for objective 1.

	MOS-HIV MHSS			GHQ score			APOS worry			APOS share		
Variable	Median score (IQR) (possible range 1-100)	Test statistic	P value	Median score (IQR) Possible range 1-12	Test statistic	p value	Median score (IQR) (possible range 0-5)	Test statistic	P value	Median score (IQR) (possible range 0-5)	Test statistic	P value
Whole sample (n=120)	44.8 (36.97-53.78)	n/a	n/a	6 (3-9)	n/a	n/a	2.5 (0-5)	n/a	n/a	5 (0-5)	n/a	n/a
Males (n=23) Females (n=97)	51.9 (41.8 – 59.1) 43.2 (36.5 – 52.0)	Mann-Whitney 2.42	0.02	5.6 6.2	Mann Whitney -0.797	0.43	0 (0-4) 3 (0.5)	Mann Whitney -1.24	0.22	5 (0-5) 5 (0-5)	Mann Whitney 0.72	0.47
Partner status Yes (n=76) No (n=44)	44.9 (36.9-54.5) 44.5 (37.0-51.1)	Mann-Whitney 0.29	0.77	6.0 6.3	Mann Whitney -0.42	0.68	3 (0-5) 0 (0-4)	Mann Whitney 1.61	0.12	5 (0-5) 4 (0-5)	Mann Whitney test 1.01	0.31
Age in years 20-29 (n=14) 30-39 (n=42) 40-49 (n=45) 50-59 (n=17) 60-69 (n=2)	40.7 (36.0-48.8) 46.3 (41.5-53.5) 45.1 (37.01-54.1) 40.2 (30.3-	Spearman's rho -0.10	0.24	4.9 6.0 5.8 7.3 11.5	Spearman's rho 0.21	0.02	1 (0-5) 2 (0-4) 3 (0-5) 3 (0-5) 2.5 (0-5)	Spearman's rho 0.10	0.26	5(3-5) 3.5(0-5) 5 (0-5) 4 (0-5) 5 (5-5)	Spearman's rho -0.004	0.96

Appendix 15 - Preliminary bivariate analysis to address objective 1

	MOS-HIV MHSS			GHQ score			APOS worry			APOS share		
Variable	Median score (IQR) (possible range 1-100)	Test statistic	P value	Median score (IQR) Possible range 1-12	Test statistic	p value	Median score (IQR) (possible range 0-5)	Test statistic	P value	Median score (IQR) (possible range 0-5)	Test statistic	P value
	54.0 27.4 (12.9-41.9)											
Wealth quintile 1 (n=27)	44.4 (38.4-36.1)	Kruskal-Wallis 0.63	0.96	6.1	Kruskal-Wallis 0.71	0.95	3 (0-5)	Kruskal-Wallis 4.02	0.40	5 (0-5)	Kruskal-Wallis 3.86	0.42
Wealth quintile 2 (n=21)	47.9 (35.5-56.7)			5.5			2 (0-5)			4 (0-5)		
Wealth quintile 3 (n=24)	44.9 (36.3-52.1)			6.2			3 (0-5)			3 (0-5)		
Wealth quintile 4 (n=24)	44.5 (40.7-51.0)			6.4			2 (0-4.5)			5 (3-5)		
Wealth quintile 5 (n=24)	45.4 (38.7-52.8)			6.2			0 (0-4)			4.5 (0-5)		
Education	41.0 (28.1-51.4)	Kruskal-Wallis 4.13	0.39	7.2	Kruskal-Wallis 3.09	0.54	3 (0-5)	Kruskal-Wallis 7.46	0.11	4.5 (0-5)	Kruskal-Wallis 1.99	0.74
Never been to school (n=10)	35.9 (31.9-44.9)			7.3			5 (5-5)			2(0-5)		
<4 yrs of school (n=3)	45.9 (36.9-55.1)			5.7			0 (0-5)			5 (0-5)		
Primary (n=76)	43.5 (39.2-51.9)			6.7			4 (0-5)			5 (0.5)		
Secondary (n=27)	44.1 (41.0-44.8)			5.8			2.5 (1-4)			4 (2-5)		

Appendix 15 - Preliminary bivariate analysis to address objective 1

	MOS-HIV MHSS			GHQ score			APOS worry			APOS share		
Variable	Median score (IQR) (possible range 1-100)	Test statistic	P value	Median score (IQR) Possible range 1-12	Test statistic	p value	Median score (IQR) (possible range 0-5)	Test statistic	P value	Median score (IQR) (possible range 0-5)	Test statistic	P value
Financial dependents	54.0 (40.2-56.1)	Spearman's rho -0.10	0.26		Spearman's rho -0.01	0.93		Spearman's rho -0.07	0.42		Spearman's rho -0.05	0.57
0 (n=9)	45.4 (36.4-52.2)						3 (0-5)			5 (5-5)		
1 (n=12)	43.7 (39.4-48.9)			5.2			3 (1.5-5)			5 (0-5)		
2 (n=14)	45.0 (41.2-54.3)			6.9			2 (0-4)			1 (0-5)		
3 (n=26)	44.7 (33.9-46.7)			6.4			1 (0-5)			1.5 (0-5)		
4 (n=12)	46.2 (35.0-53.8)			5.5			3 (0-5)			5 (0-8.5)		
5 (n=20)	44.5 (34.7-52.9)			7.1			2.5 (0-5)			5 (1.5-5)		
6 (n=13)	39.2 (37.1-41.5)			6.3			0 (0-3)			0 (0-3)		
7 (n=5)	33.3 (28.8-37.7)			5.5			0 (0-0)			5 (5-5)		
8 (n=2)	52.5 (40.2-59.5)			7.2			2.5 (0-5)			2.5 (0-5)		
9 (n=3)	45.1 (20.7-56.1)			6			0 (0-2)			4 (0-4)		
10 (n=3)	35.5 (35.5-35.5)			6			5 (3-5)			5 (3-5)		
11 (n=1)				3.7			5 (5-5)			5 (5-5)		
				8								

Appendix 15 - Preliminary bivariate analysis to address objective 1

	MOS-HIV MHSS			GHQ score			APOS worry			APOS share		
Variable	Median score (IQR) (possible range 1-100)	Test statistic	P value	Median score (IQR) Possible range 1-12	Test statistic	p value	Median score (IQR) (possible range 0-5)	Test statistic	P value	Median score (IQR) (possible range 0-5)	Test statistic	P value
Children 0 (n=16) 1 (n=22) 2 (n=26) 3 (n=20) 4 (n=10) 5 (n=15) 6 (n=5) 7 (n=4) 9 (n=1) 12 (n=1)	43.0 (39.8-52.6) 44.3 (36.5-52.2) 47.4 (41.5-56.1) 45.4 (36.1-52.4) 44.7 (30.1-46.2) 41.5 (34.1-54.1) 38.0 (30.3-41.9) 52.3 (41.1-59.8) 62.8 (62.8-62.8) 22.2 (22.2-22.2)	Spearman's rho -0.04	0.65	6.3 6.0 6.0 5.5 7.6 6.1 9 3 4 1	Spearman's rho -0.01	0.89	1 (0-5) 3.5 (0-5) 4 (0-5) 0 (0-4) 3 (0-5) 1 (0-5) 3 (0-4) 5 (0-5) 1.5 (0-4) 0 (0-0) 5 (5-5)	Spearman's rho 0.02	0.81	5 (1.5-5) 1 (0-5) 4 (0-5) 5 (0-5) 5 (0-5) 5 (0-5) 5 (5-5) 3.5 (3-4.5) 5 (5-5) 0 (0-0)	Spearman's rho 0.03	0.71
CD4 cell count at baseline		Spearman's rho -0.11	0.22		Spearman's rho 0.08	0.38		Spearman's rho 0.07	0.43		Spearman's rho -0.11	0.24

Appendix 15 - Preliminary bivariate analysis to address objective 1

	MOS-HIV MHSS			GHQ score			APOS worry			APOS share		
Variable	Median score (IQR) (possible range 1-100)	Test statistic	P value	Median score (IQR) Possible range 1-12	Test statistic	p value	Median score (IQR) (possible range 0-5)	Test statistic	P value	Median score (IQR) (possible range 0-5)	Test statistic	P value
Years since HIV diagnosis												
0 (n=26)	44.2 (36.5-48.8)	Spearman's rho -0.004	0.96	6.3	Spearman's rho -0.03	0.79	1 (0-5)	Spearman's rho 0.09	0.31	5 (1-5)	Spearman's rho -0.01	0.89
1 (n=11)	46.8 (38.0-56.7)			5.5			2 (0-5)			5 (2-5)		
2 (n=11)	41.8 (31.8-48.9)			8.1			3 (0-5)			4 (0-5)		
3 (n=17)	47.1 (41.3-57.6)			5.1			0 (0-4)			5 (2-5)		
4 (n=18)	43.2 (36.7-48.9)			6.4			0.5 (0-4)			5 (2-5)		
5 (n=23)	46.8 (37.0-54.3)			5.9			0 (0-5)			5 (0-5)		
6 (n=6)	46.8 (37.0-54.3)			7.5			5 (4-5)			5 (0-5)		
7 (n=4)	42.7 (41.2-44.9)			4.5			4.5 (3.5-5)			5 (0-5)		
8 (n=2)	43.0 (28.1-54.6)			4			3 (3-3)			2.5 (0-5)		
	42.1 (28.1-56.1)											
Years on ART												
0 (n=35)	44.8 (36.5-55.4)	Spearman's rho -0.008	0.93	6.1	Spearman's rho -0.05	0.55	2 (0-5)	Spearman's rho 0.09	0.31	5 (0-5)	Spearman's rho -0.05	0.56
1 (n=13)	41.5 (37.7-52.5)			6.4			0 (0-4)			5 (3-5)		
2 (n=20)	41.5 (37.7-52.5)			6.9			3.5 (0-5)			5 (2-5)		
3 (n=17)	44.9 (35.0-53.7)			5.2			2 (0-4)			4 (0-5)		
4 (n=14)				5			0 (0-3)			5 (5-5)		
5 (n=15)				6.2			3 (0-5)			5 (0-5)		

Appendix 15 - Preliminary bivariate analysis to address objective 1

	MOS-HIV MHSS			GHQ score			APOS worry			APOS share		
Variable	Median score (IQR) (possible range 1-100)	Test statistic	P value	Median score (IQR) Possible range 1-12	Test statistic	p value	Median score (IQR) (possible range 0-5)	Test statistic	P value	Median score (IQR) (possible range 0-5)	Test statistic	P value
6 (n=4) 7 (n=2)	45.1 (38.4-57.4) 46.1 (42.3-51.4) 44.8 (28.3-54.3) 42.2 (37.8-48.4) 32.1 (22.2-42.0)			9 3.5			5 (4.5-5) 4.5 (4-5)			5 (0-5) 5 (0-5)		
Receiving TB treatment Yes (n=10) No (n=110)	45.4 (39.0-52.9) 44.6 (36.7-54.0)	Mann Whitney 0.18	0.86	5.7 6.1	Mann Whitney -0.31	0.76	1 (0-5) 3 (0-5)	Mann Whitney -0.44	0.66	3(0-5) 5 (0-5)	Mann Whitney 0.61	0.54

